ASOCIACION MEDICA DE PUERTO RICO

BOLETIN

VOL. 74/NUM. 1 ENERO 1982

For IPPB therapy and hand nebulizer

Alupent® Inhalant Solution

(metaproterenol sulfate) 5%

long needed...long lasting

A bronchodilator for relief of reversible bronchospasm associated with bronchitis, emphysema, and bronchial asthma.

- The Solution with a long duration of action

Up to 6 hours when administered by IPPB

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- Effective for long-term use
- Adverse reactions similar to those of other sympathomimetic agents

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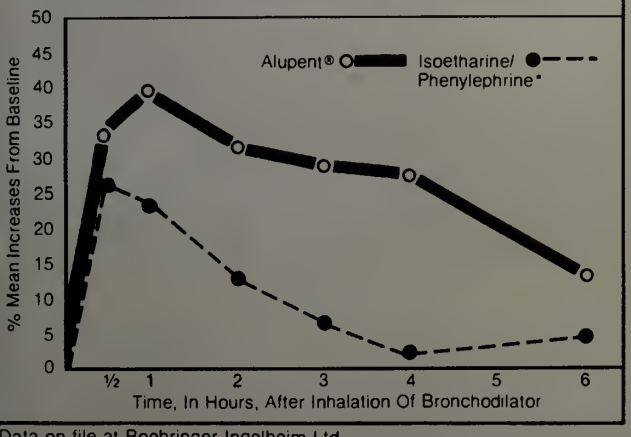

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How to use Alupent® Inhalant Solution (metaproterenol sulfate)

Method of Administration	Usual Single Dose	Frequency of Use	Range	Dilution
IPPB	0.3 ml	•For acute attacks—every 4 hrs. •For chronic bronchospastic pulmonary diseases-3 to 4 times a day.	0.2-0.3 ml	Diluted in approximately 2.5 ml of saline solution or other diluent
Hand Nebulizer	10 Inhalations	•For acute attacks—every 4 hrs. •For chronic bronchospastic pulmonary diseases-3 to 4 times a day.	5-15 inhalations	No Dilution

Please see brief summary on last page of this ad, for warnings, precautions and adverse reactions.

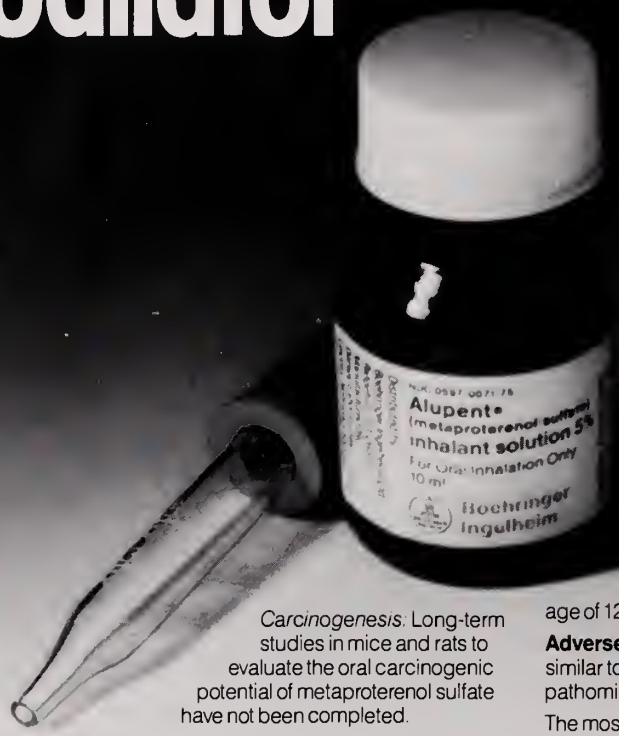
Alupent®

(metaproterenol sulfate)

Inhalant Solution

Bronchodilator

Alupent®
(metaproterenol sulfate)
Inhalant Solution
Bronchodilator



Alupent® (metaproterenol sulfate)
Inhalant Solution

Contraindications: Use in patients with cardiac arrhythmias associated with tachycardia is contraindicated.

Warnings: Excessive use of adrenergic aerosols is potentially dangerous. Fatalities have been reported following excessive use of Alupent, brand of metaproterenol sulfate, as with other sympathomimetic inhalation preparations, and the exact cause is unknown. Cardiac arrest was noted in several cases. Paradoxical bronchoconstriction with repeated excessive administration has been reported with sympathomimetic agents. Patients should be advised to contact their physician in the event that they do not respond to their usual dose of a sympathomimetic amine aerosol.

Precautions: Because Alupent, brand of metaproterenol sulfate, Inhalant Solution is a sympathomimetic drug, it should be used with great caution in patients with hypertension, coronary artery disease, congestive heart failure, hyperthyroidism or diabetes, or when there is sensitivity to sympathomimetic amines.

Information for Patients: Extreme care must be exercised with respect to the administration of additional sympathomimetic agents. A sufficient interval of time should elapse prior to administration of another sympathomimetic agent.

Carcinogenesis: Long-term studies in mice and rats to evaluate the oral carcinogenic potential of metaproterenol sulfate have not been completed.

Pregnancy: Teratogenic Effects: Pregnancy Category C. Alupent, brand of metaproterenol sulfate, has been shown to be teratogenic and embryocidal in rabbits when given orally in doses 620 times the human inhalation dose; the teratogenic effects included skeletal abnormalities and hydrocephalus with bone separation. Oral reproduction studies in mice, rats and rabbits showed no teratogenic or embryocidal effect at 50 mg/kg, or 310 times the human inhalation dose. There are no adequate and well-controlled studies in pregnant women. Alupent, brand of metaproterenol sulfate, Inhalant Solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Alupent, brand of metaproterenol sulfate, is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of Alupent Inhalant Solution in children below the age of 12 have not been established.

Adverse Reactions: Adverse reactions are similar to those noted with other sympathomimetic agents.

The most frequent adverse reactions to Alupent, brand of metaproterenol sulfate, are nervousness, tachycardia, tremor and nausea. Less frequent adverse reactions are hypertension, palpitations, vomiting and bad taste.

Overdosage: The symptoms of overdosage are those of excessive beta adrenergic stimulation listed under **Adverse Reactions.** These reactions usually do not require treatment other than reduction of dosage and/or frequency of administration.

How Supplied: Alupent, brand of metaproterenol sulfate, Inhalant Solution is supplied as a 5% solution in bottles of 10 ml with accompanying calibrated dropper. Store at room temperature; avoid excessive heat. Protect from light.

For complete details, please see full prescribing information.

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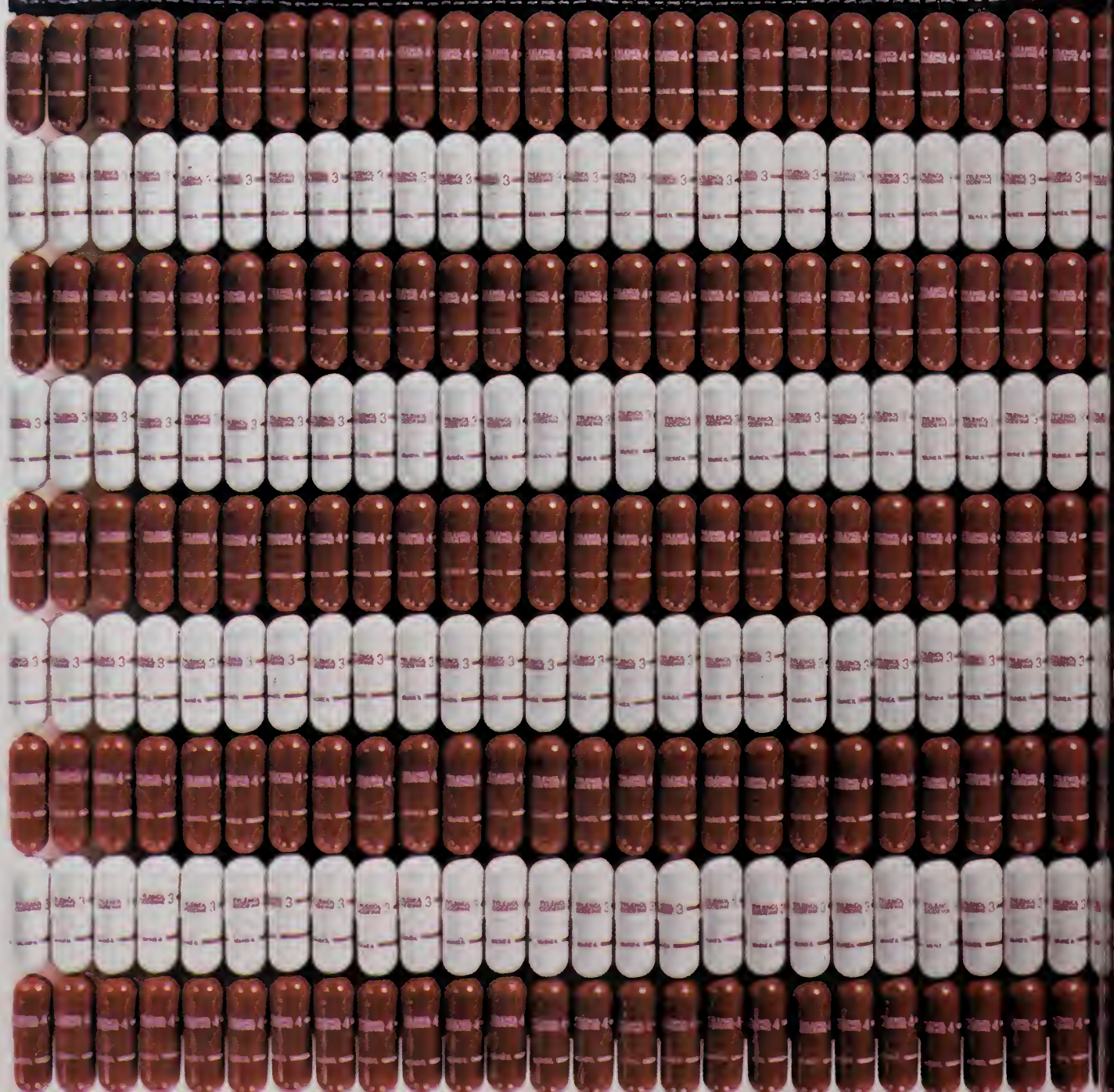

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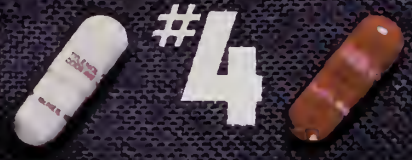

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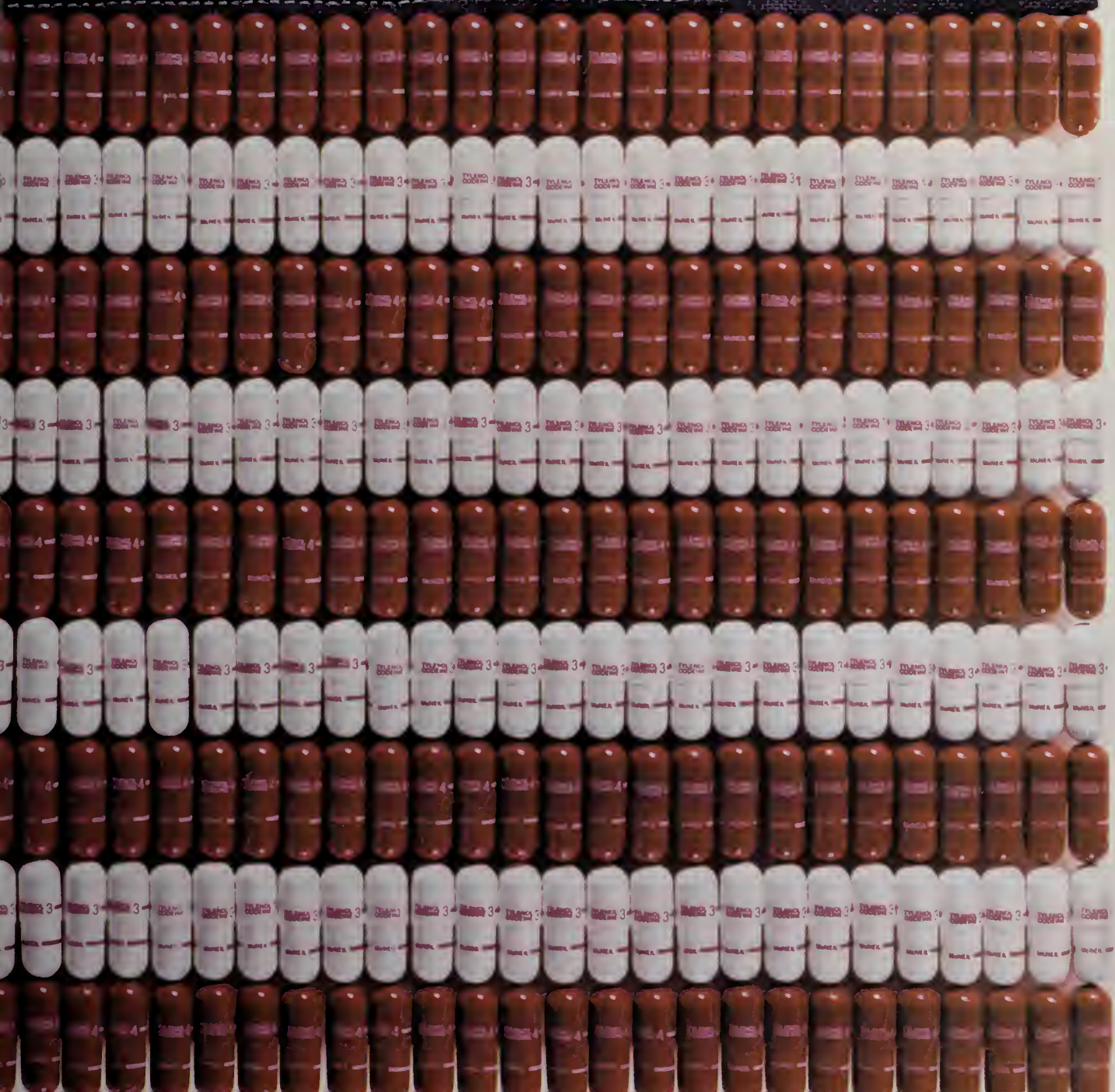

ASOCIACION MEDICA DE PUERTO RICO
BOLETIN

VOL. 74/NUM 1 ENERO 1982

NUESTRA PORTADA:

Obra en acuarela opaca en "drawing board".
Titulada "Incertidumbre".
El autor José Villavicencio captó la incertidumbre que ocasiona la llegada de un ser nuevo a un ambiente de deprivación cultural y económico desprovisto de justicia social.

José Villavicencio es puertorriqueño y nacido en Santurce. Cursó estudios en los Estados Unidos y en Puerto Rico. Es publicista y diseñador gráfico. El nuevo formato y diseño del Boletín fue posible gracias a su cooperación con la Asociación Médica de Puerto Rico.

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CONTENIDO

EDITORIAL

El Boletín de la Asociación Médica De Puerto Rico

El publicar nuestro Boletín no es tarea sencilla y desafortunadamente con el irreversible entusiasmo y dedicación de sus editores no es suficiente para lograrlo. Existen una serie de imponderables factores imprevistos que dificultan grandemente nuestra labor y que por regla general nuestros lectores están ajenos a ellos.

Antes de publicar cada número del Boletín es necesario asegurarse que esté adecuadamente impreso, perfectamente ilustrado, corregido, y presentado como corresponde a una publicación científica de calidad. Si además se añade que nuestra revista no tiene fines de lucro, que es de difusión especializada, y que no ha de llegar a la gran masa, sino a un grupo reducido de profesionales, entonces podrá comprenderse que quienes la editan tienen ante sí una ardua tarea. Si a lo anterior le incluímos un obstáculo tan difícil de salvar como la escasez de recursos económicos entonces queda poco por decir y el resultado puede fácilmente adivinarse. Generalmente estas condiciones conducen a sus creadores a dejarse sumir en la decepción que ocasionan, abandonando impotentemente la empresa.

Tal era la situación del Boletín de la Asociación Médica de Puerto Rico a principios de este año cuando su publicación se vió seriamente amenazada, precisamente cuando cumplía 79 años de existencia. Sin embargo, gracias al esfuerzo conjunto de la Junta Editora del Boletín y un comité designado por el Presidente de nuestra Asociación para lidiar con el serio problema económico, prevaleció el buen juicio, y como en toda empresa tendiente al bien colectivo se superaron los obstáculos y se establecieron los mecanismos para lograr la publicación continuada de nuestra revista. Conseguido esto, el Boletín de la Asociación Médica de Puerto Rico cumplirá su compromiso con los profesionales de la salud del país de ofrecer una continuidad en la educación médica, de proveer un medio para la publicación de los trabajos de nuestros investigadores, y servir de foro para la expresión científica de los problemas que afectan la salud de nuestro pueblo.

Hacia esos fines vamos, esperamos mejorar la presentación del Boletín, diversificar más su contenido, y poder circularlo con mayor puntualidad. Puede que en los primeros números no lo logremos, pero el deseo de superación no se extinguirá y será cuestión de tiempo el realizarlo.

Para finalizar, ya vislumbrada la superación de la "crisis" nada más oportuno que recoger las palabras del Dr. Ramón Ruíz-Arnau en el Editorial del primer Boletín de la Asociación Médica de Puerto Rico publicado en enero de 1903 luego de quedar constituida nuestra Asociación: "Se ha dado el primer paso. Ahora es preciso que el ser nacido hable, y hablará por medio de este Boletín de la Asociación Médica de Puerto Rico que viene hoy a la arena a servir de órgano y vocero para el cumplimiento de nuestros acuerdos, a recoger para su publicación la labor profesional aislada y silenciosa hasta hoy, a poner de relieve en suma, la cultura médica del país."

Para los miembros de la Junta Editora, el caer en el desaliento y abandonar la empresa ante el problema actual implicaría dar la espalda a objetivos tan nobles como los de nuestros fundadores. Reconocemos la obligación de velar por el cumplimiento de estos principios, que son la piedra angular de nuestra Asociación. Confiamos en Dios cumplir esta encomienda y que nuestra empresa refleje un positivo progreso, para que sea de un real, desinteresado, y patriótico beneficio a nuestro país.

Rafael Villavicencio, M.D.
Presidente, Junta Editora
Boletín Asociación Médica de Puerto Rico
Abril 1982

estudios clínicos

CARCINOMA OF THE PROSTATE: CONTROL OF PELVIC TUMOR BY RADIOTHERAPY

Víctor A. Marcial, MD
José M. Tomé, MD
Jeanne Ubiñas, MD
L.V. Marcial-Vega, MS IV

Summary: **Carcinoma of the prostate has become the leading cancer in Puerto Rican males and its incidence continues increasing.**

With the aim of determining the efficacy of radiation therapy to the diesease in the pelvis, a restrospective review of patients with stage A, B, and C treated at the Radiotherapy Institute of the Metropolitan Hospital during the period July 1972 to December 1978 was conducted.

One hundred and five patients with disease clinically limited to the pelvis received irradiation during the stated period. Radiotherapy controlled the desease in the pelvis in 84 percent of the patients. Fifty percent of patients survived 5-years. Ninety three percent of 5-year suvivors were free of tumor.

The complication rate, pelvic tumor control and survival achieved are comparable to those reported in the medical literature.

We advise early radiotherapy for clinically evident carcinoma of the prostate limited to the pelvis. Needle biopsy of the prostate should be used as the preferred diagnostic method, inasmuch as transurethral resection increases the incidence of radiation complications. Hormonal therapy should be avoided until definitive evidence of distant metastasis is available.

Introduction

Carcinoma of the prostate has shown a constant increase in incidence in Puerto Rico in the last quarter century and has become the leading form of cancer in males. Data from the Puerto Rico Central Cancer Registry reveal that from the year 1950 to the year 1978 the number of cases registered per year increased by 600 percent. Table I shows the crude incidence rate increased from 5.7 cases per 100,000 males per year in 1950 to 27.4 in 1978 (450 cases). The age related incidence expressed in cases per 100,000 males per year ranged from 2.86 per 100,000 males in the 45 to 49 age group to 277.6 in the 70-74 age group. The registry data also showed that 67.7 percent of cases had disease localized or limited to the prostate, that the percentage of histologically proven tumor was 86.9 percent, and that the percentage of cases without definitive treatment to the disease was 20.4 percent.

In the past the treatment of carcinoma of the prostate was restricted to a small sample of cases (less than 5.0 percent of patients) who could be submitted to prostatectomy. Because of this limited applicability of surgery some surgeons have been led to believe that carcinoma of the prostate is a hopeless disease that does not deserve to be treated.

The present report relates to an analysis of our experience with patients presenting with carcinoma of the prostate, clinically limited to the pelvis, who underwent curative radiotherapy. The objective is to determine the effectiveness of this therapeutic modality in controlling the tumor in the pelvis. We also report on the survival achieved after therapy.

Materials and Methods

The case histories of patients with the diagnosis of carcinoma of the prostate referred to the Radiotherapy Institute of the Metropolitan Hospital in San Juan, Puerto Rico during the period July 1972 to December 1978 were reviewed. A research data manager from the Radiotherapy division of the University of Puerto Rico School of Medicine, and a medical student from the same institution, participated in this analysis of data. Information was tabulated on each case taking into consideration age, prior therapy, stage of disease, histologic diagnosis, type and dose of radiotherapy, results of radiotherapy in terms of control of tumor in the pelvis, and complications related to therapy, and survival, The stanging used is shown in Table II. All patients had histologically proven tumor. Besides physical examination, patients were submitted to chest radiograph, bone survey and/or radioiostope bone scan, I.V.P., C.B.C., urinalysis, SMA 12, and serum acid phosphatase determination.

Patients without information on the status of the pelvic tumor during follow-up were assumed to have pelvic disease in the evaluation of this parameter. The calculations of tumor control in the pelvis and the survival were made by the direct statistical method.

Results

During the period July 1972 to December 1978 a total of 190 patients were registered with the diagnosis of carcinoma of the prostate at the Radiotherapy Institute of the

From the Radiation Oncology Division, University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

This project was supported in part by grants No. R 10 CA-12258-09 and 5 P30 CA-16598-06 from the National Cancer Institute.

Metropolitan Hospital. The stage distribution of these cases is shown in Table III. The patients who had the disease limited to the pelvis and who were candidates for pelvic irradiation were 123 of which 15 did not receive treatment at the institution, 3 had incomplete therapy and 105 had complete radiotherapy at the Radiotherapy Institute. The age distribution of the group of 105 cases who had complete radiation is shown in Table IV. The youngest was 50 years of age and the oldest 88, with a median age of 72. Only 8 percent of patients were younger than 60 years of age. The stage distribution of these 105 patients is: A-1, B-2, C-99, and D_1-3.

Treatment

The treatment administered to these cases was cobalt teletherapy with anterior and posterior fields ranging in size from 14 x 14 to 15 x 15, supplemented with lateral or rotational portals. The total dose to the pelvis was approximately 5000 rad calculated in the central axis of the beam at the level of the midpelvis, with daily fractions of 180 to 200 rad delivered 5 times per week. After the stated pelvic irradiation a boost was administered to the prostate with a reduced field, for a total dose to this organ of 6600 to 7000 rad in 6 1/2 weeks. In some cases a rest period of one to two weeks was permitted between the pelvic irradiation and the prostate boost.

TABLE I

Carcinoma of the Prostate in Puerto Rico
Crude Incidence Rates

	Cases/100,000 Males
1950	5.7
1955	8.4
1960	12.4
1965	12.3
1970	19.9
1975	25.9
1978	27.4

TABLE II

Stage Classification

State	
A	MICROSCOPIC (NO PALPABLE) TUMOI
B	PALPABLE TUMOR NOT EXTENDING BEYOND CAPSULE
C	EXTENDS BEYOND CAPSULE OR TO SURROUNDING STRUCTURES
D_1	TUMOR IN PELVIC NODES
D_2	TUMOR OUTSIDE PELVIS

Control of Tumor in the Pelvis

In Table V one can note the control of tumor in the pelvis achieved by the end of therapy and at each year, up to 5 years after the first day of therapy. In 84 percent of cases radiotherapy achieved complete disappearance (C.R.) of the tumor in the pelvis. Because of the small number (28) of cases qualifying for 5 year evaluation and the fact that patients dead, or known to be alive but not coming to follow-up, are assumed to have pelvic disease, the C.R. is only 46 percent at 5 years. In patients known to be alive (Table VI) the control of tumor in the pelvis at 5 years is 93 percent.

TABLE III

Carcinoma of Prostate
Radiotherapy Institute-Metropolitan Hospital
July 1972 to December 1978

Total Cases Registered		190
Stage Distribution:		
A	—	2
B	—	7
C	—	106
D	—	68
Previous Treat.	—	7
Total-		190

TABLE IV

AGE DISTRIBUTION

YOUNGEST	50
OLDEST	88
MEDIAN AGE	72

PERCENTAGE DISTRIBUTION

	No. Cases	Percent
Below 60	9	8
60 - 69	34	32
70 - 79	53	50
80 Over	9	9
Total-	105	

Complications

Radiotherapy to the pelvis resulted in complications in 26 percent of 95 patients with available information (Table VII). The most frequently reported complication was

TABLE V

Tumor Control in Pelvis
All Cases

Interval After Day 1*	No. Pts. Eligible	No. with No Tumor in Pelvis**	% NED***
Initial	105	88	84
1 Year	100	77	77
2 Year	86	58	67
3 Year	62	35	56
4 Year	46	23	50
5 Year	28	13	46

* - First Day of Therapy.
** - No Palpable Tumor in Pelvis.
*** - NED - No Evidence of Tumor.

Patients without information are assumed to have pelvic tumor.

proctitis with bood in the stools in 8 cases, followed by uretheral stenosis requiring surgical dilatation in 5 patients, and cystitis with blood in the urine in 4 cases. Serious complications, which is one considered to be life threatening or needing a surgical procedure, was reported in 3 percent of patients. The patients who developed recto-sigmoid complications requiring colostomy deserve some discussion.

TABLE VI

Tumor Control in Pelvis
Living Patients

Interval After Day 1*	No. Pts. Eligible	No. with No Tumor in Pelvis**	% NED***
1 Year	95	77	81
2 Years	69	58	84
3 Years	40	35	87
4 Years	26	23	88
5 Years	14	13	93

* - First Day of Therapy.
** - No Palpable Tumor in Pelvis.
*** - NED - No Evidence of Tumor.

Patients without information are assumed to have pelvic tumor.

TABLE VII

Complications

Type	No. of Cases
Proctitis with Blood in Stools	8
Urethral Stenosis Needing Dilatation	5
Cystitis with Blood in Urine	4
Needed Colostomy	2
Other Types of Complications	6
Reported Complications of all Types and Degree:	29/95-26%
Incidenceof Serious Complications:	3/95-3%

TABLE VIII

Carcinoma of the Prostate Limited to the Pelvis
Absolute Survival* 105 Cases

Interval From Day 1**	Pts. Eligible	Patients Alive	% Survival
1 Year	100	95	95
2 Years	86	69	80
3 Years	62	40	64
4 Years	46	26	56
5 Years	28	14	50

* - Direct Method.
** - First Day of Therapy.

One was a 61 years old man who 12 years before had received irradiation to the spine for Hodgkin's Disease, had suffered form lues, had infection and ligation treatment for hemorrhoids, and received a dose of 7000 rad in 51 days with a telecobalt rotational technique. It is conceivable that syphilis may have altered his vascular status and that the irradiation for Hodgkin's Disease may have contributed to the complication. The other case, a 74 years old man who had pelvic surgery (suprapubic prostatectomy) and incisional hernia, was treated with a stationary telecobalt technique to a dose of 5000 rad in 39 days to the entire pelvis. This was followed by a 10 day rest period, and then a boost with rotational therapy for a dose of 2000 rad in 2 weeks. The pelvic surgery may have contributed to the complications by fixing a loop of bowel and making it more sensitive to radiotherapy.

TABLE IX

Carcinoma of the Prostate
All Stages
Survival*

Years	% Survival
1	69.9
3	46
5	32.9
No. of Cases:	2,386

* P.R. Cancer Registry

Survival

The absolute survival achieved in this group of cases form the first day of therapy is shown in Table VIII. This ranged from 95 percent at 1 year to 50 percent at 5 years.

Distant Metastases

By the time of this report 23 percent (24 of 105) of cases had developed distant metastases. These metastases made their appearance by 2 years in 33 percent of cases, by 3 years in 63 percent, and by 4 years in 83 percent. The chances of developing distant metastases by the end of the first year after therapy are 9 percent, by 2 years 19 percent, and by 3 years 22 percent.

Discussion

Because of aging of the population and other unknown factors, carcinoma of the prostate has become the leading cancer problem in Puerto Rican males. It is expected that the observed yearly increase in incidence will continue as more males enter the advanced age groups.

Some urologists are of the opinion that cancer of the prostate deserves no treatment, for they believe that therapy will not alter the ultimate outcome of the disease. This is unjustified, for except in early stage A cases with well differentiated histology, the untreated tumor is expected to continue growing locally, and producing lymph node and distant metastases. Castration alone, and/or estrogen therapy, does not produce lasting effect that may improve survival.[7] Contrarywise, hormonal therapy at certain dose levels may reduce survival.[11] It has been reported that untreated stage C carcinoma of the prostate has a 3-year survival of 22 percent.[7] The Puerto Rico Cancer Registry has reported a 3-year survival of 46 percent (Table IX) for all stages of the disease. Our series showed that 64 percent of

patients survived 3 years, but it is noteworthy that 87 percent of surviving patients were free of tumor in the pelvis, even though in patients without information we assumed the presence of pelvic tumor. One has to conclude from these data that radiation therapy improves the survival of patients with carcinoma of the prostate whose disease is clinically limited to the pelvis when treated.

Reports from the medical literature by del Regato[3], Bagshaw[1], and others[4 5 6 8 9] reinforce the concept that the treatment of carcinoma of the prostate with radiation is justified. These authors have reported 5-year survival rates ranging from 58.8 percent to 86.8 percent for stage B, and 40 to 58 percent for stage C.[4 5 9]

Long-term control of prostate carcinoma with radiation therapy have been reported by Regato[3] and Bagshaw[1]. The latter has reported direct survival rates at 10 years of 42 percent ofr patients with neoplasm limited to the prostate and 29 percent for those with extracapsular extension.

Radiotherapy should be administered in the first few months after diagnosis, for a delay longer than 6 months may reduce the survival by half[5].

Complete radiation induced regression of a palpable prostate tumor is a lengthy process. At Johns Hopkins, it has been reported that complete regression of the palpable disease in stage B cases ocurred in only 27 percent of cases by the sixth month. Eighteen months were required for 74 percent of the tumors to regress[6]. Consequently, biopsy to determine status of tumor in the first 2 years after therapy is a worthless effort.

Complications with any therapeutic regime is a reality in medicine and radiotherapy of prostate cancer is no exception. Taylor[9] reports 40 percent incidence of mild dysuria and hematuria, of which 3 percent were classified as severe. We observed 26 percent incidence of all types and 3 percent severe complication. However, we know that previous transurethral resection (T.U.R.) is a predisposing factor. Taylor[9] advises a waiting period of 3 to 6 weeks after TUR and 6 weeks after prostatectomy before initiating radiotherapy. The energy of radiation, besides the total dose, has also been considered an important factor; linear accelerator therapy should result in a lower percentage of complications. Stanford reduced the overall complication rate from 30 percent to 14 percent with a change in treatment technique[8]. At Johns Hopkins Hospital they have found of value the use of a rest period between the pelvic irradiation and the prostate boost[8]. At he present time most of our patients rest one to two weeks between pelvic irradiation (5000 rad in 5 to 6 weeks) and the prostate boost with reduced fields (1600 to 2000 rad). We expect that the complication rate will be reduced in our patients with the use of the linear accelerator, the introduction of a rest period between pelvic irradiation and the prostatic boost, and the increasing use of needle biopsy instead of TUR as a diagnostic procedure.

The high incidence of distant metastases after pelvic therapy of primary prostatic cancer is a disturbing finding. Advanced stage of the primary tumor, the presence of positive lymph nodes, and poor differentiation of the tumor are all associated with a high probability of developing distant metastases. Para-aortic lymph node irradiation is being investigated by the Radiation Therapy Oncology Group with the aim of reducing this problem. Adjuvant chemotherapy is also being investigated by various groups with the same purpose.

Early diagnosis and treatment are the best promise for the improvement of prognosis in prostate cancer. Annual rectal palpation of the prostate in males 40 years of age or older will permit diagnosis when the disease in confined to the prostate (stage B). When the tumor extends beyond the capsule (stage C) the incidence of distant metastases exceeds 50 percent.

Surgery, by the perineal or retropublic approach, has been practiced at some centers[2 6]. This has been limited to discrete and small nodules usually not larger than 1.5 cm in diameter.[2] Prostatectomy is associated with an impotency rate of 85 to 90 percent and a high incidence of urinary incontinence.[6 7] Impotence is less a problem in patients treated with radiation therapy. Sexual function following irradiation can be maintained in 59 to 69 percent of patients.[8]

Resumen: El carcinoma de la próstata es actualmente el tumor maligno más frecuente en el hombre puertorriqueño y su incidencia continúa avanzando cada año.

Se presenta un estudio retrospectivo de los pacientes con estadíos A,B y C tratados en el Instituto de Radioterapia del Hospital Metropolitano en San Juan, durante el período de julio 1972 a diciembre 1978; con el propósito de determinar la efectividad de la radioterapia en controlar el tumor en la pelvis.

Un grupo de 105 pacientes con enfermedad limitada a la pelvis recibió irradiación durante el período mencionado. La radioterapia logró controlar el tumor en la pelvis en 84 por ciento de los pacientes. La sobrevida a 5 años fue de un 50 por ciento. Los pacientes que sobrevivieron 5 años mostraron un control del tumor en la pelvis, por la radioterapia, de 93 por ciento.

La incidencia de complicaciones, control del tumor en la pelvis y la sobrevida observados en este grupo de pacientes es comparable a la de otros estudios en la literatura médica.

Se recomienda el manejo temprano con la radioterapia en tumores de la próstata que están limitados a la pelvis (A_2, B, C y D_1). La biopsia por aguja se asocia a menor incidencia de complicaciones que la transuretral. La terapia hormonal se debe reservar para la etapa en que se tenga prueba de enfermedad a distancia.

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Ms. Raquel Santos typed the manuscript and Ms. Lydia López, R.N. was data manager.

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VARICEAL BLEEDING A REVIEW OF A RECENT EXPERIENCE

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Summary: Our experience in the management of 22 cirrhotic patients admitted during a period of one year bleeding from varices is reviewed. Ten had hypotension on admission and 15 had an initial hematocrit less than 30%. Seventeen had moderate to severe hepatic dysfunction on admission. Uncontrolled bleeding was the cause of death in six of eight (36%) who died during the hospitalization. A brief review of recent therapeutic developments in this condition is made.

Variceal bleeding (VB) is one of the most serious illnesses in medicine. A recent cooperative prospective study reported an in-hospital mortality of 30% in patients admitted with this diagnosis.[1]

This review was undertaken to evaluate our experiences in the management of this clinical problem and to determine the efficacy of the present techniques in managing this condition. A brief review of the literature was made of VB with emphasis on the experience at other centers, the rationale for the present techniques of management and recent advances in this field.

Materials and Methods

The records of 22 patients admitted to this institution during calendar year 1980 with a diagnosis of VB were reviewed. Variceal bleeding was diagnosed if one of the following criteria was fulfilled: 1. the endoscopist reported seeing active bleeding from the varices or a blood clot overlying a varix and no other lesions; 2. endoscopy was not performed but at autopsy varices and blood in the stomach and gut were only found; 3. endoscopy was not performed but the patient had evidence of massive bleeding from the upper gastrointestinal tract on admission (fresh flood was aspirated through a nasogastric tube and the hematocrit on admission was less than 30%) and in addition active bleeding from varices had been described by an endoscopist two weeks before at the time of a previous admission.

Hepatic functional reserve was estimated by the Child's criteria.[2]

Results

Nineteen of the twenty-two patients were actively bleeding from varices or had a blood clot overlying a varix and no other mucosal lesion to explain the bleeding.

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The median age of the patients was 54 years (range 34 to 66). Forty-five percent of the patients had massive blood loss on admission. Sixty-eight percent of the patients had an initial blood hematocrit less than 30%. Seventy-seven prcent had hematemesis just prior to admission.

As can be seen in Table 1, 77% of the patients had moderate to severe hepatic dysfunction as estimated by Child's criteria. Only five patients were Child's class A on admission.

Twenty patients received blood transfusions. A total of 102 units of blood were transfused (median number of transfusions was 4). In addition, 29 units of resh frozen plasma were transfused. The two patients who were not transfused were not actively bleeding at admission, did not rebleed during the hospitalization, and their initial hematocrits were 39 and 37%.

Vasopressin was administered by continuous peripheral vein infusion in nineteen patients. The maximum rate of vasopressin infusion was 0.3 units per minute.

The Linton or the Sengstaken-Blakemore compression tubes were used in seventeen occasions in thirteen patients. These tubes were used when vasopressin infusions failed to stop the variceal bleeding. Adequate control of bleeding occurred in eight, temporary control in four and no control of bleeding in five. One of the thirteen patients was intubated three times due to recurrence of bleeding and perforation of the esophagus was found at autopsy.

The in-hospital mortality was 36% (eight patients). Persistent, uncontrollable variceal hemorrhage was the cause of death in six of these patients. Two died from multiple organ failure.

Ten patients were actively bleeding on admission. The in-hospital mortality in this subgroup was 50%. Four of the five patients who died in this group had uncontrollable hemorrhage.

Four patients had surgery during the hospitalization. None of these patients died (three were Child's class B, and one was class A). One of the operations was performed as an emergency and three were done electively.

The median lenght of hospitalization was 16.5 days (range: 1 to 60 days).

Discussion

One of every three patients admitted with a diagnosis of VB died. This experience compares favorably with other reports. In eight large series reported from 40 to 90% with a mean mortality of 65% for the 1123 patients evaluated.[3-11] Koransky et al[11] reported a 32% mortality in 62 patients evaluated retrospectively and in whom the diagnosis of blee-

ding from varices was made endoscopically or at autopsy. The ASGE (American Society for Gastrointestinal Endoscopy) prospective evaluation reported a 30% mortality in patients with VB.[1]

Six of our patients died from uncontrollable bleeding (75% of those who died). The experience reported by other authors has been similar. In Koransky et al's series[11] seventy percent died from persistent bleeding. In Baker et al's report[12] seventy-nine percent died from this complication.

The mortality associated with VB is higher than for most other causes of upper gastrointestinal bleeding. In the ASGE study[13] the overall mortality associated with upper gastrointestinal bleeding was 10.8%. In patients with actively bleeding varices the mortality was 36.2% while in patients with varices but who were not actively bleeding on admission the mortality was 18.6%. The overall mortality in patients with varices was 30.1%. Patients who bled from duodenal ulcers had an overall mortality rate of 6.7%. The mortality rates for gastric ulcers was 7.8%, for Mallory-Weiss tears was 4.4%, for gastric erosions was 9.8% and for neoplasm was 17.2%.

A number of factors in addition to the site of bleeding, are associated with an increased risk of dying in patients admitted with upper gastrointestinal bleeding. Age is important. Avery Jones[14] reported in 1956 that patients bleeding from peptic ulcers less than 60 years of age had a mortality rate of 3% while patients older than 60 had a mortality rate between 12 and 47%. Another factor is recurrence of bleeding. Avery Jones[14] reported a ten fold increase risk of dying in patients with peptic ulcers who rebleed during the admission. Some of the other factors associated with a significantly higher risk of dying include: previous history of cardiac arrhytmia, congestive heart failure, myocardial infarction, acute and chronic encephalopathy, stroke, liver failure, alcoholic hepatitis, hematologic or solid-type malignancy, chronic obstructive pulmonary disease, pneumonia, and renal failure.[13]

Our patients received the standard medical therapy which included blood volume replacement, vasopressin infusions, and the use of compression tubes. In addition, four patients underwent surgery during the admission.

Vasopressin has been used since the 1950's. Kehne et al[15] reported control of variceal bleeding in two patients treated with a posterior pituitary extract (Pituitrin) by peripheral intravenous infusion (ten to twenty units were administered over five to ten minutes). Merigan et al [16] performed a controlled study evaluating the efficacy of intravenously administered posterior pituitary extract in cirrhotic subjects with VB. Fifty-five percent of the patients who received the pituitary extract had at least temporary control of bleeding as compared to 0% of the control group. The mortality was, neverthless, similar in both groups. Interest in vasopressin was renewed when Nusbaum et al[17] compared the effects of vasopressin with other pharmacologic agents. These authors infused the superior mesenteric artery of dogs and reported that vasopressin reduced the portal pressure without significantly altering the cardiac output. Other pharmacologic agents such as epinephrine, norepinephrine and angiotensin induced portal outflow resistance and increased portal pressure. This led to the evaluation of intraarterial infusions of vasopressin in several clinical trials. Conn et al[18] reported that selective arterial infusion of vasopressin at a maximum infusion rate of 0.4 units/minute arrested bleeding in 71% of variceal bleeeding episoded as compared to cessation of bleeding in 25% of the controls. More recent studies[19 20] have shown no significant difference in control of variceal bleeding or mortality when vasopressin is infused continously through a peripheral vein or by selective infusion of the superior mesenteric artery. The intravenous administration is presently recommended because the effects and complications are similar to the intraarterial route and the intravenous administration is technically more simple. The usually recommended dose of intravenous vasopressin is 0.3 units per minute.[20] Coronary artery disease, myocardial ischemia or infarction are some of the contraindications to vasopressin therapy.

Compression tubes have been used to treat VB for more than twenty-five years. Sengstaken and Blakemore[21] described the use of balloon tamponade in 1950. Nachlas[22] reporte control of bleeding in ten of thirteen patients. The success rates of control of VB with compression tubes have varied widely in the reported literature. Effective control of hemorrhage has ranged from about 40% to 92%.[23 24] A number of factors have been proposed to explain the observed variability. The selection of patients treated is one factor. For example, in one study balloon tamponade was used only if vasopressin therapy[23] failed. These patients had been bleeding longer, had required more transfusions prior to the utilization of the compression tubes and had failed to respond to other medical therapy. These factors are all associated with a worse prognosis.[25 26]. Variation in the definition of control of bleeding, in the documentation of VB, and in the type of compression tube used are some of the factors which explain the reported experience.[1 25 26]

Surgery has been one of the standard therapeutic modalities available for patients with varices. Prophylactic shunts, that is, shunts performed in patients with varices but who never bled from varices, should not be performed according to he available evidence. Resnick et al[27] did a prospective, controlled evaluation of prophylactic portocaval shunts in 93 patients with cirrhosis and esophageal varices. Survival was about 45% in the surgical and the control groups after eight years of follow up and the frequency of portosystemic encephalopathy was higher in the surgical group. Conn and Lindenmuth's controlled evaluation of the prophylactic shunt also found no evidence that surgery improved survival (56% in the surgical group and 68% in the control group).[28]

There is no uniform agreement about the efficacy of the therapeutic shunt, that is, shunts performed electively following at least one documented episode of variceal bleeding. Jackson et al[29] and Mikkelsen[30] have reported controlled clinical trials of the portocaval shunt in such patients. They reported significantly better survival rates in the surgical group as compared to the control group. Re-evaluation of Jackson's study by Conn[31], however, suggests that there was no significant difference in the survival rates between the two groups. Resnick[32] and Reynolds[33] have reported controlled clinical trials in which there was no difference in the cumulative survival between the shunted and the unshunted patients.

Shunts performed in patients who are acutely bleeding from varices have a reported operative mortality which ranges from 23 to over 70%.[34 38] None of these reports evaluated the outcome of concomittant unshunted control patients. Controlled clinical trials are therefore needed to define the

role of emergency surgery in variceal bleeding.

End to side portocaval shunts were performed in most of the surgical studies cited previously. Newer surgical procedures such as the distal splenorenal shunt and the Sugiura procedure may change the postoperative prognosis and make surgical intervention desirable. Zeppa et al[39] reported in 1978 an operative mortality of 1% in 91 patients who had therapeutic distal splenorenal shunts. These authors also reported a five year survival frequency of 89% in the nonalcoholic cirrhotics operated as compared to 39% for the alcoholic patients. Sugiura and Futagawa[40] reported in 1977 the operative mortality associated with the Sugiura procedure (which involves performing esophageal transection, para-esophagogastric devascularization and splenectomy) in 276 patients. The operative mortality was 11.5% in fifty-two patients sho had the procedure performed as an emergency, 1.8% in one hundred sixty-four patients who had therapeutic intervention and 5% in sixty patients sho had prophylactic surgery. New controlled trials should be performed to evaluate the effect-iveness of these new surgical procedures in variceal bleeding.

In the past decade several reports have appeared describing the obliteration of varices by percutaenous transhepatic catheterization of the portal vein with selective catheterization of the coronary and short gastric vein followed by injection of a sclerosing agent.[41] [44] The initial report by Lunderquist and Vang[41] described the technique in four patients, two of whom were actively bleeding from varices. Injection of hypertonic dextrose and thrombin thrombosed the coronary vein and stopped bleeding in the two actively bleeding patients. Viamonte et al[44] reported their experience in seventy-three patients, thirty-two of whom were actively bleeding from varices. Varices were obliterated in sixty-seven patients. Recurrence of variceal bleeding ocurred in nine of the sixty-seven patients. Bengmark et al[43] reported their experience with this technique in forty-three patients. Of fourteen patients actively bleeding from varices twelve were controlled for at least one day following the injection. Eight of these twelve patients day following the injection. Eight of these twelve patients rebled at a later date. In addition, ten of the forty-three patients (23%) suffered complications due to the procedure, seven of them fatal.

Endoscopic injection of varices with sclerosing agents has also been tried in the management of variceal bleeding.[45] [46] Terblanche et al[45] recently reported control of variceal bleeding in 92% of twenty-two patients. These patients had needle injection of varices under general anesthesia through a rigid esophagoscope.

Clark et al[46] conducted a prospective trial of endoscopic injection of varices in sixty-four cirrhotics who had recently bled from varices. Sclerotherapy was performed in thirty-six patients and twenty-eight patients received suportive therapy only. Rebleeding was significantly more frequent in the control group (86% versus 33%). One year survival rate was 65% in the injection group and 46% in the control group. There was one death attributable to sclerotherapy. Ten patients receiving sclerotherapy developed esophageal ulceration and four of these developed esophageal strictures which responded to dilatation. These preliminary injection sclerotherapy studies are interesting but further controlled clinical evaluations will be required to establish the efficacy and safety of injection sclerotherapy in the prevention of recurrence of variceal bleeding.

Addendum

After this article was submitted for publication Lebrec et al. reported the results of a controlled study of propranolol in the prevention of re-bleeding in patients with cirrhosis who had bled from esophageal or gastric varices or acute gastric erosions (N Engl J Med 1981; 305: 1371-4). Thirty-seven of thirty-eight patients (96%) in the propranolol group were free of recurrent gastrointestinal bleeding one year after inclusion in the study as compared to 50% of the patients in the placebo group. The authors concluded that because of its efficacy and lack of serious side effects propranolol (given in a dose that reduces the heart rate 25%) is recommended for prevention of re-bleeding in cirrhotics who are otherwise in good health. They warned, however, that the efficacy of propranolol in cirrhotics with poor liver function is unknown.

TABLE I

Characteristics of the Patient Population (N=22)

Age:	median - 54 (range 34 to 66)
Sex:	all males
Previous admissions variceal bleeding:	11 (50%)
Massive blood loss:*	10 (45%)
Child's class:**	A - 5
	B - 14
	C - 3
Jaundice:	13
Ascites:	6
Encephalopathy:	4

* Estimated at admission if the systolic BP was less than 90mm Hg supine or postural hypotension was documented.
** See Materials and Methods.

Resumen: La experiencia adquirida durante un año en el manejo de 22 pacientes cirróticos ingresados con sangría por varices ha sido revisada. En 10 hubo hipotensión y en 15 el hematocrito inicial fue por debajo de 30%. En 17 se encontró disfunción hepática moderada o severa al ingreso. La sangría incontrolable fue la causa de muerte en 6 de 8 enfermos que murieron. La literatura médica reciente sobre este tema ha sido revisada.

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presentación de casos

CRUSTED (NORWEGIAN) SCABIES

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Summary: **Crusted (Norwegian) scabies is an unusual skin infestation by the mite Sarcoptes scabies distinguished from the common form of scabies by the presence of remarkable hyperkeratotic lesions teeming with mites. This condition has been reported in a variety of clinical settings and the potential of a ward epidemic exists if the diagnosis is not made early in the condition. The authors report 3 cases of crusted (Norwegian) scabies emphasizing its clinical characteristics and forms of diagnosis which should enable the clinician to make an early diagnosis and therefore prevent potential hospital epidemics of scabies.**

Introduction

Uncommon in the 1950's scabies has progressed in frequency since 1964 to epidemic proportions worldwide.[1,3] Although it was thought that the epidemic would subside in 1979, our current clinical experience indicate that this is far from true. In the United States scabies constitutes 2 to 4 percent of patients seen in dermatologist offices[4]. Although there are no exact figures in Puerto Rico, the current epidemic is probably at its peak in the island, judging by the number of new cases diagnosed every day in dermatology clinics.

In the current cycle, classical scabies is seen less frequently. Special forms, especially minimal scabies in clean persons are common and more difficult to diagnose. Still, there are some other clinical presentations which pose an increased threat of infestations to others.

Crusted or Norwegian scabies is an unusual skin infestation by the mite Sarcoptes scabies, distinguished from the common form of scabies by the presence of remarkable hyperkeratotic lesions teeming with mites (5-12). Since this type of the condition has usually been reported in a variety of clinical settings, the potential of a ward epidemic exists if the diagnosis is not made early in the condition.

The purpose of this communication is to report 3 cases of Norwegian scabies which have been evaluated in our institution emphasizing its clinical characteristics and forms of diagnosis which should enable the clinician to make an early diagnosis and therèfore prevent potential hospital epidemics of scabies.

Report of Cases

Case 1:

An 8 year-old white female patient with systemic lupus erythematosus of three years duration had been hospitalized for two months at the University Children's Hospital because her condition was complicated with lupus nephritis, right pleural effusion, pericardial effusion, anemia, leukopenia and hypertensive crisis and was receiving treatment with methylprednisolone 58 mg p.o daily, methyldopa one gram p.o. daily, spironolactone 25 mg p.o. daily, Cephalotin sodium 80 mg p.o.q. 6 hrs. and was on a drip of sodium nitroprusside.

The dermatology service was consulted because she complained of mild pruritus and the appearance of multiple scaly papules and plaques on her body for the last week. The patient's mother recalled a similar episode about one year ago which resolved with topical medication successfully.

The physical examination disclosed a chronically ill, cushingoid female girl in no acute distress. Her blood pressure was under adequate control and positive physical findings at the time of consultation included moon facies, central obesity, ascites, splenomegaly and muscle wasting.

On the skin, the patient exhibited multiple tiny 2-3 mm scaly erythematous papules located over the trunk and extremities. On the dorsum of her feet near the interdigital areas, there were several scaly hyperkeratotic erythematous plaques (Figs. 1 and 2). Skin scraping from these plaques were seen under the light microscope with mineral oil and showed hundreds of eggs, adult Sarcoptes scabies organisms and cibala. A punch biopsy from one of these plaques was performed.

The patient and her mother were treated with gamma-benzene hexachloride lotion successfully. Ward personnel was examined but no active cases were found. Special precautions were taken in handling bed clothes of the patient.

Case 2

A 94 year-old female patient who came from a nursing home was admitted because of severe dehydration. She had history of peptic ulcer disease and organic brain syndrome. Two months before, the patient had developed multiple scaly plaques on the palms and soles, with associated erythema and scaliness over the body. The patient was treated before admission with systemic steroids orally and topically and with antihistamines orally to no avail. She had ankylosis of the vertebral column and most of the time lied immobile in bed in fetal position.

Physical examination showed a chronically ill, cachetic female patient lying in fetal position with ankylosis of the extremities. She was disoriented in time, place and person and also incoherent.

The skin examination showed large scaly plaques on the palms, arms and some areas of the trunk. There were multiple tiny scaly erythematous papules and burrows through out the skin.

From the Department of Dermatology, Medical Sciences Campus, University of Puerto Rico, San Juan, Puerto Rico 00936.

The skin scraping showed multiple adult mites, ova and cibalas of Sarcoptes scabies. A punch biopsy was performed from one of the lesions. The patient was treated effectively with gamma-benzene hexachloride lotion and shampoo, and ward nurses were notified about precautions in handling bed clothing. One nurse who started with itching but without skin lesions was treated prohylactically with gamma-benzene hexachloride lotion successfully.

Figure 1: Appearance of the skin lesions on the right foot. (Case 1).

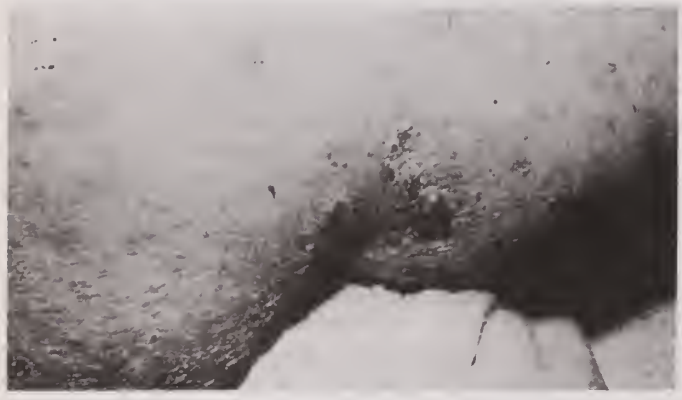

Figure 2: Crusted hyperkeratotic plaques on right lower extremity (Case 1).

Case 3

A 60 year-old female was admitted to the hospital because of a persistent generalized skin eruption which had been unresponsive to multiple topical medications and systemic corticosteroids. The skin eruption started with itching and scaling on the abdominal area followed by progressive involvement to other areas of the trunk, face and extremities. The had 2 previous hospitalizations to other institutions three months prior to admission.

The patient had past history of craniotomy in 1959 for plastysbasia. In 1970, she developed dysphagia, dysphonia and progressive atrophy and contracture of the fingers of the left hand accompanied by cervical spine pain and numbness and paresthesia of both hands. Skull series showed a very large (7 cms) and wide bony defect at the inferior aspect of the occipital bone down to the foramen magnum in association to platysbasia. Electroencephalogram revealed an abnormal resting tracting with generalized slowning. Spinal tap and brain scan were within normal limits. A cervical laminectomy was performed at that time with improvement of the symptomatology.

On admission, the physical examination revealed a chronically ill elderly female in no acute distress. Skin examination revealed erythematous thick scaly plaques on the chest, back, abdomen and scalp with relative sparing of the lower extremities and hands.

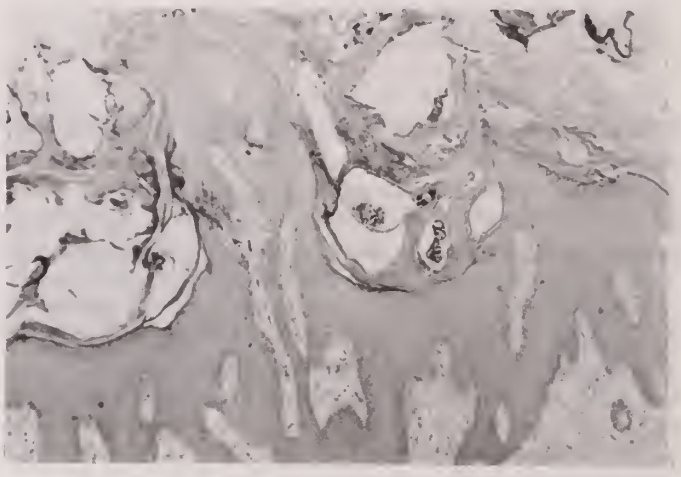

Figure 3: Acanthotic epidermis with interdigitating rete ridges showing abundant adult mites, larvae, ova and fecal matter within compartments of hyperkeratotic horny layer. There are increased and dilated capillaries in the upper dermis with a mixed infiltrate. (H and E, x 10).

Other pertinent findings in the physical examination included a short neck with a surgical scar in the posterior area of the neck with some limitation of movement but no neck rigidity. There was mild atrophy of the upper and lower extremities with ulnar claw hands and interosseous atrophy of both hands. The shoulders were asymetric. There was some limitation of movement of the upper extremities and focal areas exhibited decreased light touch. Graphestesia and stereonosia were decreased in the left hand.

Skin scraping form the lesions revealed multiple adult mites, ova and cibalas of Sarcoptes scabies. A punch biopsy was also performed.

She was treated successfully with gamma-benzene hexachloride lotion.

Histopathology

Histopathological findings were similar in the 3 cases. The epidermis showed adult mites, larvae, nymphs, ova and fecal matter in abundance lodged within compartments of hyperkeratotic and crusted cornified layer. The epidermis was markedly acanthothic with interdigitating rete ridges. There were increased and dilated capillaries in the upper dermis with an infiltrate consisting of lymphocytes, histiocytes and eosinophils. (Figures 3 and 4).

Comments

Norwegian scabies was first described in Norwegian lepers in 1848 by Danielssen and Boeck[6]. Cases have since been reported in a variety of clinical settings usually involving chronically ill institutionalized patients[7 8]. Mentally retarded patients, especially with Down's syndrome, have a high incidence of Norwegian scabies[8 9], although the reason of this propensity is unclear. Immune deficient patients such as those with lepromatous leprosy and immune suppressed patients,

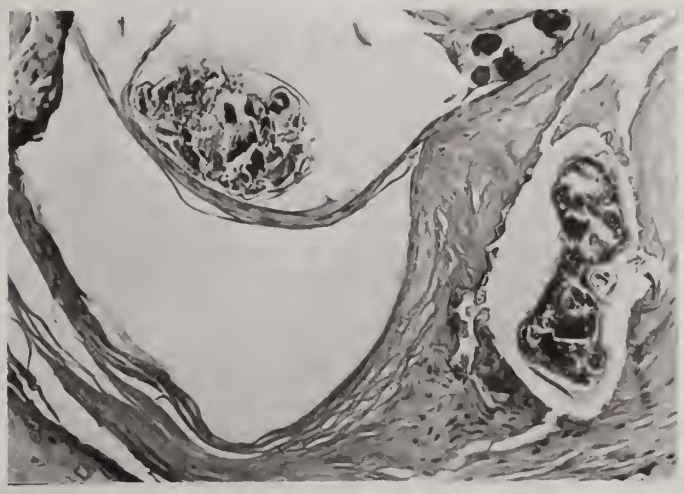

Figure 4: Adult mites and larvae within the stratum corneum. (H and E, x 40).

usually following renal transplantation and/or during therapy with corticosteroids and/or azathioprine, also have developed this peculiar eruption.[9-10] Topical corticosteroid therapy can also alter the local host response so that Norwegian scabies appears.[11 12] Cases have also been reported in association with chronic malnutrition and avitaminosis, severe infections, diabetes and leukemia.[13] Crusted scabies is also observed in some nervous diseases which produce analgesia, such as syringomyelia in which a lowering of immunity is less evident.[13] In these particular cases, the absence of pruritus is probably sufficient to produce this syndrome.

Our three cases presented with conditions in which Norwegian scabies have been associated previously. Case 1 is an immunosuppressed child with SLE treated with oral steroids for 3 years. Case 2 is a debilited postrated elderly female with organic brain syndrome with possible diminished cutaneous sensation and Case 3 is a patient with platysbasia with diminished motor function and a very mild sensory deficit who could not scratch normally due to her neurologic disease. Also, another predisposing factor in cases 2 and 3 is that they were previously treated with topical and systemic steroids which may have modified the host local response permitting the proliferation of organisms in the lesions[11 12].

Norwegian scabies differ from classic scabies by the hyperkeratotic, scaly and crusted aspect of the lesions. The extent of lesions varies but the scaling, infiltration and redness are often widespread. The most characteristic lesions are seen at the extremities, where keratotic excrescenses are often produced. The neck, the face and the scalp may also be involved by the scaling, and alopecia may occur. Burrows are generally present. The pruritus is characteristically mild or absent[14]. The mites are always extremely abundant in the lesions and there may be upward of 2 million adult mites in the crusts[15].

Cases of crusted scabies are highly contagious and they have often been the source of hospital epidemics. Wells[16] reported that 67 cases of scabies occurred among patients and nursing staff infested by a single patient with crusted scabies. In none of these secondary cases did the diseases developed into crusted scabies. Intensely itchy papules were present in all the patients. In most of the cases the symptomatoloty was atypical, in that the burrows were very rare and the lesions were generally not located in the classic sites but appeared in places which had been in contact with the source of infestation.

Crusted scabies is often mistaken for atypical psoriasis, seborrheic dematitis, erythroderma, chronic mucocutaneous candidiasis and many other dermatologic disorders. In many cases the patient has spread the disease before the diagnosis has been made.

Crusted scabies is more frequently observed in patients 65 or older than in young people, but epidemics have been reported in patients ranging in age from 12 to 20, all physically and mentally handicapped; the majority with Down's Syndrome.[17]

The reason why scabies evolves into the crusted type in some persons is not completely understood but there appear to be several mechanisms. Both the host's immune response and the character of the skin may be important in modifying the response to the scabies mites. The appearance of Norwegian scabies in patients with iatrogenic immune suppression, such as renal transplant patients, and with natural deficiencies, such as lepromatous leprosy, supports this concept. Localized immunosuppression, as produced by topical applications of glucocorticosteroids, has been associated with the appearance of Norwegian scabies.[11 12]

Crusted scabies is also observed in some nervous diseases which produce analgesia and diminished cutaneous sensation such as syringomegalia in which a lowering of immunity is less evident.[13] In these particular cases, the absence of pruritus and/or the inteference with scratching are probably sufficient to produce the syndrome.

Diagnosis of the condition is easily made by identifying unexcoriated papules or burrows. Mineral oil is placed on a sterile scalped blande and allowed to flow on the skin lesions. Vigorous scraping with the blade removes the top of the papules or burrows. The oil and scraped material are transferred to a glass slide and covered with a cover slip. Identification of any stage of the mite under low power microscopy is diagnostic. Also skin biopsy of the lesions can provide identification of the numerous organisms present within the thickened stratum corneous as seen in the present cases.

Therapy for Norwegian scabies similar to that for the more common forms is usually sufficient, although this type responds more slowly and may require repeated applications.[5] Gamma-benzene hexachloride cream or lotion is easy to use and the most effective treatment. Crotamiton and sulfur are alternative medications.

In summary, three cases of Norwegian scabies presenting characteristic clinical and histologic findings have been presented. This form of scabies is highly infectious and usually presents in debilitated chronically ill patients, in others undergoing immunosuppressive therapy and in others with underlying neurologic disorders. Early suspicion in a hospitalized patient with rapid confirmation by skin scraping or by skin biopsy should help prevent potential ward epidemics of scabies.

Resumen: **La escabiosis costrosa es una infestación de la piel poco frecuente causada por el ácaro Sarcoptes scabies. Esta se distingue de la escabiosis común por la presencia de lesiones hiperqueratocicas bien prominentes que contienen numerosos organismos. La condición se ha reportado mucho en pacientes hospitalizados existiendo el riesgo de epidemias si el diagnóstico se demora. Los autores presentan 3 csos de escabiosis costrosa enfatizando las características clínicas y formas de diagnóstico de la condición que ayudan a hacer un diagnóstico temprano y evitar epidemias hospitalarias de la condición.**

* References will be submitted upon request to the author.

FORO DE MEDICINA NUCLEAR

DIAGNOSTIC IMAGING IN STRESS FRACTURE

Jaime J. Rivera MD
Bert E. Mason, DPM
Paul J. Anderson, MD

The diagnosis of bone fractures has traditionally been substantiated by radiographic findings. The sensivity of this diagnostic modality has been disappointing in the early detection of fractures. A clinical example is fractures of the scaphoid bone.[1] This is even more dramatic in stress fracture where initial radiographs may be normal. Scintigraphic imaging can frequently be helpful in the early detection of fractures in difficult areas and when stress fractures are suspected. Early detection of stress fractures could prevent further damage and the subsequent need for long term immobilization.

In a military institution where basic military training occurs the stress placed on the trainees during physical exercise and conditioning produces numerous complaints of pain in the lower extremities. The physician faces the dialemma of determining which patients are suffering from early stress fractures and which from functional stress. Initial radiographs are of little benefit to the physician, thus making the diagnosis even more difficult.

Case Summary

Case 1:

A 24-year old white male, National Guard basic trainee, was referred with a chief complaint of pain in the right hand for 6 weeks and no history of injury. Initial X-rays were negative as were follow up X-rays 6 weeks later. A bone scan (Fig. 1A) was performed which demonstrated a focal area of intense uptake in the scaphoid bone of the right hand.

Case 2:

A 32-year old white male, National Guard basic trainee, was referred with a chief complaint of right ankle and left knee pain for 3 weeks and no history of injury. Initial radiographs were negative. A bone scan (Fig. 2A) was then performed which showed intense focal uptake in the left medial tibial plateau and distal right tibia. Repeated radiographs (Figs. 2B and 2C) one week after the bone scane demonstrated sclerotic changes in these areas.

From the Department of Radiology and the Nuclear Medicine Service Ireland Army Hospital, Fort Knox, Kentucky.

Figure 1: Bone scan (A) demonstrates an intense focal uptake in the scaphoid one of the right hand (arrow).

Case 3:

An 18-year old white male, basic Army trainee was referred from the Podiatry Clinic with a chief complaint of left foot pain of 2 weeks duration without a history of trauma. Initial radiographs were negative. A bone scan (Fig. 3A, B) was performed and demonstrated focally increased uptake in the area of symptoms as well as in other unsuspected areas ("shin splints").

Case 4:

A 21-year old white female, a ROTC Cadet, was referred with a chief complaint of right heel pain which started in her third week of training. Initial radiographs were negative. Because of persistent pain, a bone scan was requested (Fig. 4A). it shows a well defined focal area of increased uptake in the right calcaneous. Repeated radiographs two weeks after shows a sclerotic region in the area corresponding to the abnormal bone scan findings (Fig. 4B).

Discussion

Bone scanning is most commonly used on the detection of metastic bone disease. Extensive clinical experience has been obtained for more than three decades using this

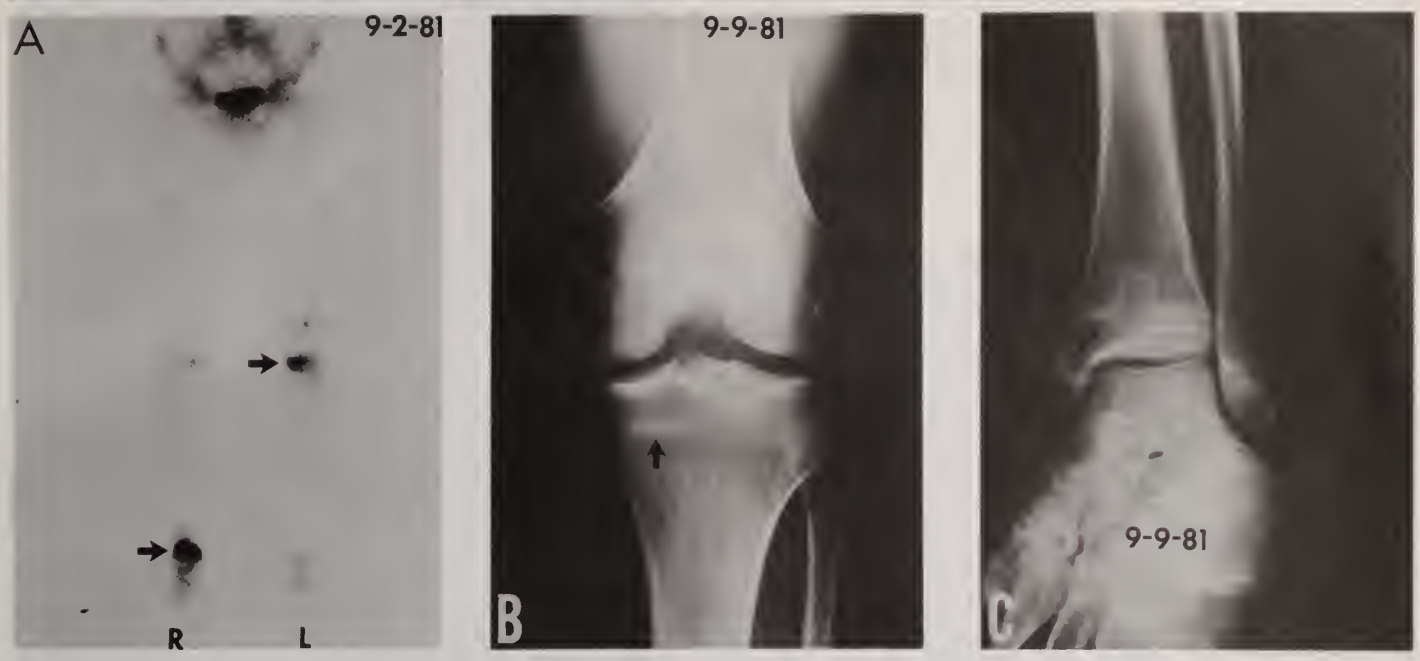

Fig. 2: Bone scan (A) demonstrates intense uptake in the left medial tibial plateu and distal tibia (arrows). Radiographs (B and C) were normal initially and when repeated one week after the bone scan, demonstrate sclerotic changes (arrows) in the corresponding areas of abnormal uptake in the bone scan.

procedure. At present bone-seeking agents are eing used for the evaluation of skeletal metastases, primary bone tumors, infections, aseptic necrosis, skeletal trauma, joint disorders, metbolic bone disease, Paget's disease, and it's extraosseous localization[2]. It is also being used for acute myocardial injury detection, localization and sizing.

The radiopharmaceuticals used today are technetium 99m labeled phosphates and phosphonates. The mechanism of localization involves an exchange of these compounds with the inorganic components of hydroxyapatite, $Ca_{10}(PO_4)_6(OH)_2$, the principal mineral in the skeleton. After the intravenous injection, a major fraction (40 percent - 60 percent) is accumulated by the skeleton while most of the remainder is excreted by the kidneys into the urine. The images are obtained usually after two hours of injection. The total body radiation absorbed dose is less than 300 mrads and that to the skeleton is less than 500 mrads. The critical organ in regard to radiation is the urinary bladder and for that reason the patient is instructed to consume liquids and void frequently.

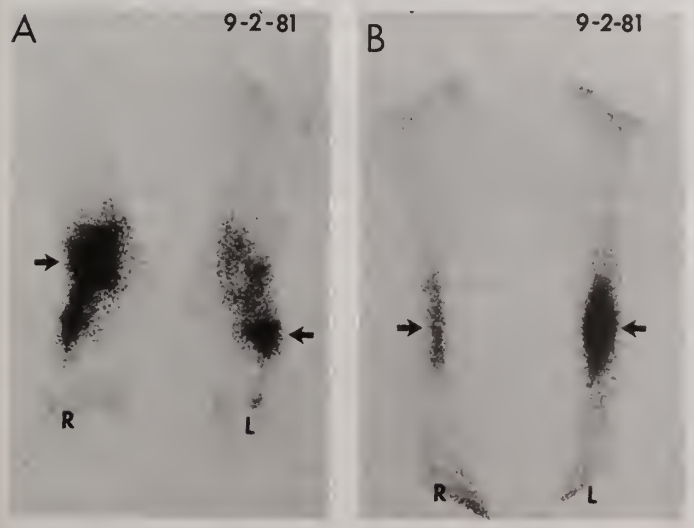

Fig. 3: Bone scan (A) demonstrating a stress injury of the right ankle (arrow). Unsuspected bilateral mid tibia stress fractures (B) (arrows).

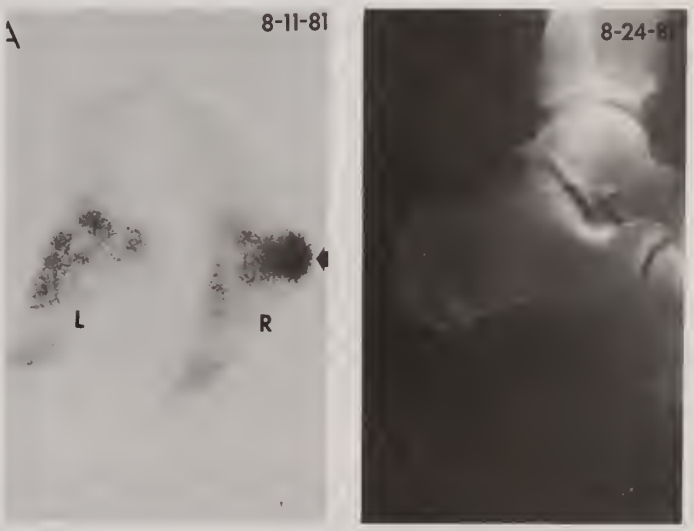

Fig. 4: Bone scan (A) demonstrates an intense focal area of increased uptake (arrow) in the right calcaneus. Radiograph (B) showing sclerotic changes (arrow). This is the most common abnormality seen in our service.

Traumatic fractures are usually the result of an acute isolated event and are detected by conventional radiographs. This is not true for stress fractures. This type of bone injury appears to be part of a continuum of events. The majority of the cases demonstrate no abnormal findings with conventional radiographs in the initial films. Some of them will demonstrate changes later on and many have no changes at all.[3]

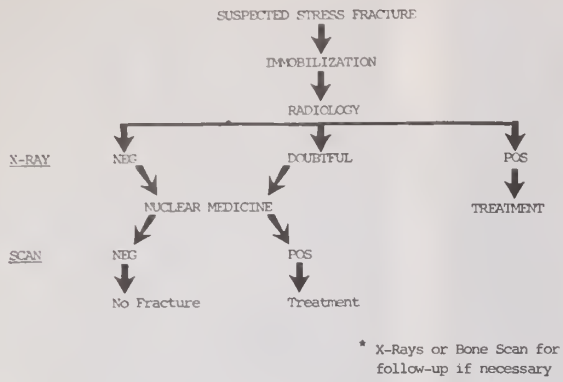

Fig. 5 Suggested approach in the evaluation of suspected stress fractures.

In stress fractures, a focal area of increased tracer uptake can be detected as early as 24 hours, and if negative beyond 3 days, it virtually excludes fractures.[4] The bone scan is very sensitive to any metabolic bone activity and therefore other processes will demonstrate similar findings. For example, periosteal tear without fracture can produce a positive bone scan.

In the illustrative examples the bone scan findings were crucial in the proper management. The detection of stress fractures is the most common indication for bone scanning in our institution. Figure 5 explains our present approach in the evaluation of suspected stress fractures. In the civilian world, joggers and those involved in other physical activities may require this approach in the evaluation of pain. In our opinion, bone scanning offers a new perspective in the practice of clinical medicine.

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INDICATIONS: *Therapeutically* (as an adjunct to systemic therapy when indicated), for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically,* the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.

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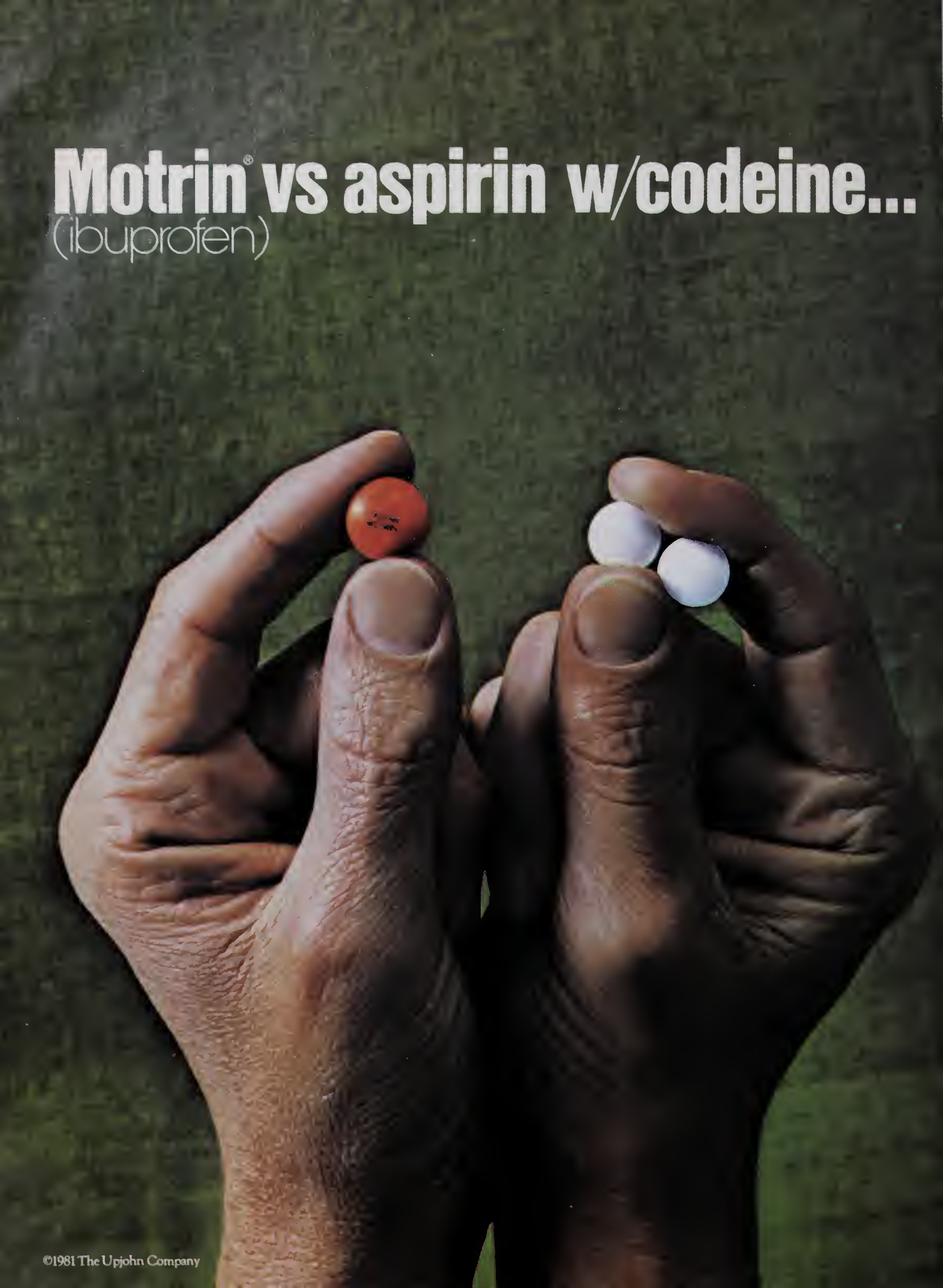
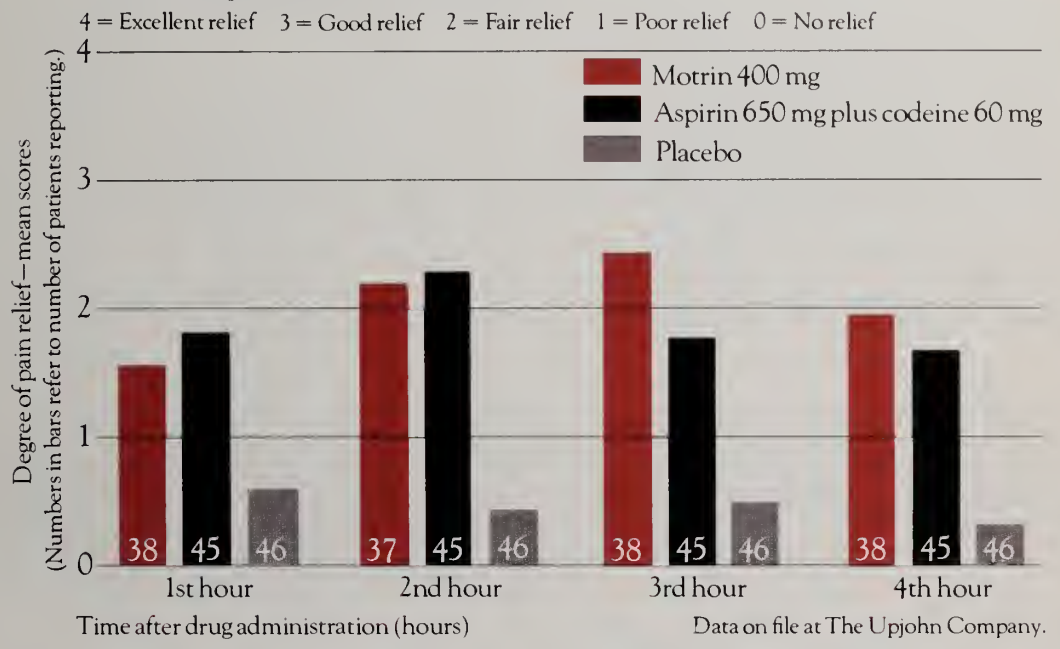
Motrin® vs aspirin w/codeine...
(ibuprofen)



compare the analgesic effect

A *Motrin* 400 mg dose relieved postsurgical dental pain as effectively as a combination of 650 mg aspirin and 60 mg codeine (two aspirin-with-codeine No. 3 tablets) in a study of 129 patients. In this double-blind, placebo-controlled, randomized study, no statistically significant difference in relief of pain was noted at 1, 2, and 4 hours between the *Motrin* and aspirin-with-codeine groups... with *Motrin* being significantly more effective ($p = 0.03$) at the three-hour interval. Active treatment was significantly more effective ($p < 0.0001$) than placebo at all time intervals.

Comparison of pain relief
Motrin vs aspirin-codeine combination



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Contraindications: Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

Warnings: Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.

Drug interactions. *Aspirin:* Used concomitantly may decrease Motrin blood levels. *Coumarin:* Bleeding has been reported in patients taking Motrin and coumarin.

Pregnancy and nursing mothers: Motrin should not be taken during pregnancy nor by nursing mothers.

Adverse Reactions

Incidence greater than 1%

Gastrointestinal: The most frequent type of adverse reaction occurring with Motrin is gastrointestinal (4% to 16%). This includes nausea,* epigastric pain,* heartburn,* diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness,* headache, nervousness. **Dermatologic:** Rash* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

*Incidence 3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

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MARCH 1981

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It's a myth that arthritis is just the minor aches and pains of old age. It's a major crippler that attacks. Anybody. Anytime. 31 million Americans have it. There are almost a million new cases a year. And six out of ten are under 60. Symptoms can come and go for years. So if you don't know the warning signals, find out. If you'd like information that could help you—or you'd like to help us—write to the Arthritis Foundation, Box 19000, Atlanta, GA 30326.

ARTHRITIS FOUNDATION

auto evaluación

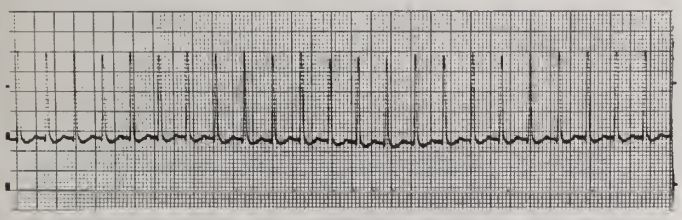
CASOS DE ELECTROCARDIOGRAFIA PEDIATRICA

Rafael Villavicencio, MD

LVB es un infante de 4 meses de edad, nacido con un peso adecuado para su edad gestacional, y producto de un embarazo de 39 semanas sin complicaciones. No había historial materno de diabetes, desbalance electrolítico, ni enfermedad cardíaca. El parto fue espontáneo, por vía vaginal y sin complicaciones.

Tuvo una estadía normal en la sala de recién nacidos y a los 4 meses de edad desarrolló taquipnea (100/min), taquicardia (240/mın), y discreta cianosis circumoral. No había soplo significativo y los pulsos periféricos estaban presentes en todas las extremidades. El ionograma, la glucemia, y la hemoglobina eran normales, al igual que la radiografía de tórax.

El electrocardiograma no demostró hipertrofia de cámaras, el eje QRS era normal, y se obtuvo la derivación II que se ilustra a continuación:



El diagnósitco corecto es:

a) taquicardia supraventricular
b) aleteo ("flutter") atrial
c) taquicardia ventricular
d) fibrilación atrial
e) taquicardia ventricular

Respuesta: a) Taquicardia Supraventricular

La taquicardia supraventricular (TSV) es la taquidisritmia más frecuente en niños, incluyendo al neonato, y ocasiona síntomas la mayoría de las veces. Su incidencia se reporta como de 1:25,000 niños, basada en un estimado hecho en 1967.[1] Sin embargo, 15 años más tarde debemos tener en mente que los medios para su detección se han mejorado, y se está más consciente de su presencia. Durante este tiempo también ha aumentado el número de niños que son sometidos a cirugía cardíaca, siendo la TSV una de las secuelas post-operatorias más frecuentes. Por estas razones se cree que en la actualidad la incidencia de TSV en niños es mayor de lo que se estimaba en 1967.

Criterios Diagnósticos

La taquicardia supraventricular en un electrocardiograma de superficie se caracteriza por:

1. Frecuencia cardíaca de 200 a 300/min., dependiendo de la edad del paciente. En el neonato la frecuencia media en TSV es de 290/min.[2]
2. Ritmo regular (intervalos R-R regulares).
3. Complejos QRS normales.
4. La onda P usualmente no está visible. En algunas ocasiones le sigue al QRS y a veces está sobreimpuesta a la onda T.
5. Tiene comienzo y terminación súbita.

Mecanismo

En un estudio reciente, utilizando métodos invasivos como el electrograma del haz de His, marcapasos atriales y creando extraestímulos atriales se logró identificar los mecanismos responsables en la producción de esta disritmia.[3]

Los mecanismos observados fueron:

1. Por reentrada al nodo A-V — el más frecuente.
2. Reentrada a través de una vía accesoria anormal [síndrome de Wolff-Parkinson-White (WPW)].
3. Reentrada a través de un fascículo A-V accesorio. En el ECG de superficie se traduce como: intervalo PR corto; QRS normal, y ausencia de la onda delta. Es el síndome de Lown-Ganong-Levine.
4. Reentrada por un tracto accesorio de conducción AV oculto.
5. Reentrada al nodo sinusal.
6. Por un foco atrial ectópico automático.
7. Taquicardia no-paroxística juncional - son períodos de ritmo sinusal alternado con episodios de ritmo juncional a una frecuencia cardíaca más rápida.

El estudio citado ilustra la diversidad de mecanismos en la génesis de la TSV. La identificación del mecanismo específico es de gran importancia para el manejo de estas taquidisritmias, ya que de acuerdo a éste se seleccionará la terapia que ha de ser más efectiva en suprimir esta taquidisritmia.

Análsis del Trazado

El trazado muestra:

— frecuencia ventricular de 240/min.
— intervalos R-R regulares.
— complejos QRS normales.
— ondas P no visibles.

Además, hay una discreta (1.5 mm) depresión del segmento ST que se normalizó una vez al paciente revirtió al ritmo sinusal normal.

Factores Predisponentes

La mayoría de los niños con TSV tienen por lo demás un corazón normal. Los factores que más frecuentemente predisponen a taquidisritmias son:

1. Síndrome de pre-excitación (Wolff-Parkinson-White).
2. Cardiopatías congénitas, sobre todo:
   a) anomalía de Ebstein
   b) inversión ventricular
   c) prolapso de la válvula mitral
3. Historial familiar — un historial familiar positivo de TSV es más frecuente que uno de cardiopatías congénitas. En parientes de primer grado la incidencia es de un 6 por ciento la cual es mayor que para cardiopatías congénitas.
4. Edad — es más frecente en niños menores de 4 meses. En los pacientes en que la TSV apareció en o antes de los 4 meses de edad se encontró que:
   a) desarrollaban una frecuencia cardíaca mayor durante el episodio.
   b) la mayor parte desarrollaba fallo cardíaco congestivo.
   c) las recaídas a largo plazo eran menos frecuentes.
   d) había una incidencia mayor de WPW.
   e) habían menos factores predisponentes presentes.
5. Cirugía cardíaca — las más frecuentes fueron el procedimiento de Mustard para la reparación de transposición de grandes vasos y luego de la reparación de defectos interatriales.
6. Medicamento simpatomiméticos
7. Miocardiopatías.
8. Sepsis.
9. Bebidas estimulantes.
10. Tensión emocional.

Tratamiento

En su etapa inicial tiene función terapéutica y diagnóstica. Mientras se instaura el tratamiento de la fase aguda debe determinarse la presencia de algún factor predisponente.

Tratamiento Agudo

1. Maniobras vagales
   a) masaje unilateral del seno carotídeo.
   b) maniobra de Valsalva — en infantes puede lograrse haciendo presión sobre el estómago.
   c) inducción de vómito.

Pueden intentarse estas maniobras en sucesión pero probablemente sean inefectivas en niños menores de 4 años.

   Inmersión facial — la inmersión facial en agua helada (5° a -15° C) por 5 - 10 segundos ha sido efectiva suprimiendo la TSV.[4] Esta maniobra resulta en un estímulo vagal fuerte, es efectiva en infantes, pero debe tenerse la precaución de cerrarle la boca y taparle la nariz al niño para evitar la aspiración. Puede hacerse también colocando súbitamente una bolsa de hielo en la cara del paciente.
3. Cardioversión — es exitosa en la mayoría de los casos. La dosis de energía inicial recomendada es de 0.25 Joules (watt-sec)/Kg. Se puede ir aumentando en incrementos de 1 Joule/Kg.

Si el paciente para conversión tienen niveles terapéuticos de digoxin pueden inducirse disritmias ventriculares por lo que debe administrarse lidocaína antes de la cardioversión como medida profiláctica.

4. Propranolol — si las medidas anteriores no son efectivas éste puede administrarse por vía endovenosa en un bolo de 0.10 mg/Kg en 15 min. Se debe vigilar el paciente para hipotensión y bradicardia.
5. Digoxin — puede usarse en niños con TSV que están menos afectados. La dosis total es de 0.04 a 0.05mg/Kg. (máximo de 0.8 mg) administrado IV y dividido en tres dosis a intervalos de 6 horas.
6. Verapamil — es un derivado sintético de la papaverina con propiedades antiarrítmicas. Usados desde la década del 60 en países de Europa y Sur América pero de inclusión reciente (1981) en el mercado Norteamericano. Es muy efectivo en el control de TSV por mecanismos de reentrada.[5]

Tratamiento a Largo Plazo

Luego de controlar el episodio inicial de TSV debe comenzarse el tratamiento crónico de todos los casos por lo menos por espacio de un año. La experiencia indica que la TSV repite en muchos niños existan o no factores predisponentes; sin embargo, estas recaídas son significativamente menos frecuentes en pacientes con tratamiento crónico.

Los medicamentos más utilizados son:

1. Digoxin — debe ser el mediacamento a utilizar de primer intención en todos los casos con TSV sin WPW y en infantes menores de un año irrespectivo de si hay WPW o no. La dosis de mantenimiento oral es 25 por ciento de la dosis total inicial y debe administrarse en dosis divididas dos veces por día.
   No debe usarse en pacientes mayores de 1 año con WPW a menos que se compruebe por estudios electrofisiológicos intracardíacos que el período refractario efectivo del tracto accesorio no se acorta al inyectarse experimentalmente vabaína.
2. Propranolol — es especialmente efectivo en pacientes con TSV y disociación A-V. La dosis usual es de 2 a 6 mg/Kg/día dividido en 4 dosis. El nivel sérico mayor se obtiene entre 1 y 2 horas luego de su administración oral

y se requieren niveles de mantenimiento entre 80 a 150 ng/ml para la supresión efectiva de disritmias ventriculares crónicas.

El uso combinado de propranolol y digoxin es un método frecuentemente utilizado en el manejo a largo plazo de la TSV.

3. Quinidina — es especialmente efectiva en pacientes con TSV por WPW al combinarla con digoxin o propraholol. Se prefiere el sulfato de quinidina a base de 30 - 40 mg/kg/día dividido en 4 dosis. Es importante mantener las concentraciones séricas a niveles adecuados para obtener un efecto antiarrítmico óptimo.

Tratamiento quirúrgico

Se recomienda en aquellos caso con TSV resistente al tratamiento médico cuando hay un tracto accesorio de Kent. En estos pacientes sintomáticos se extirpa el Haz de Kent.[6]

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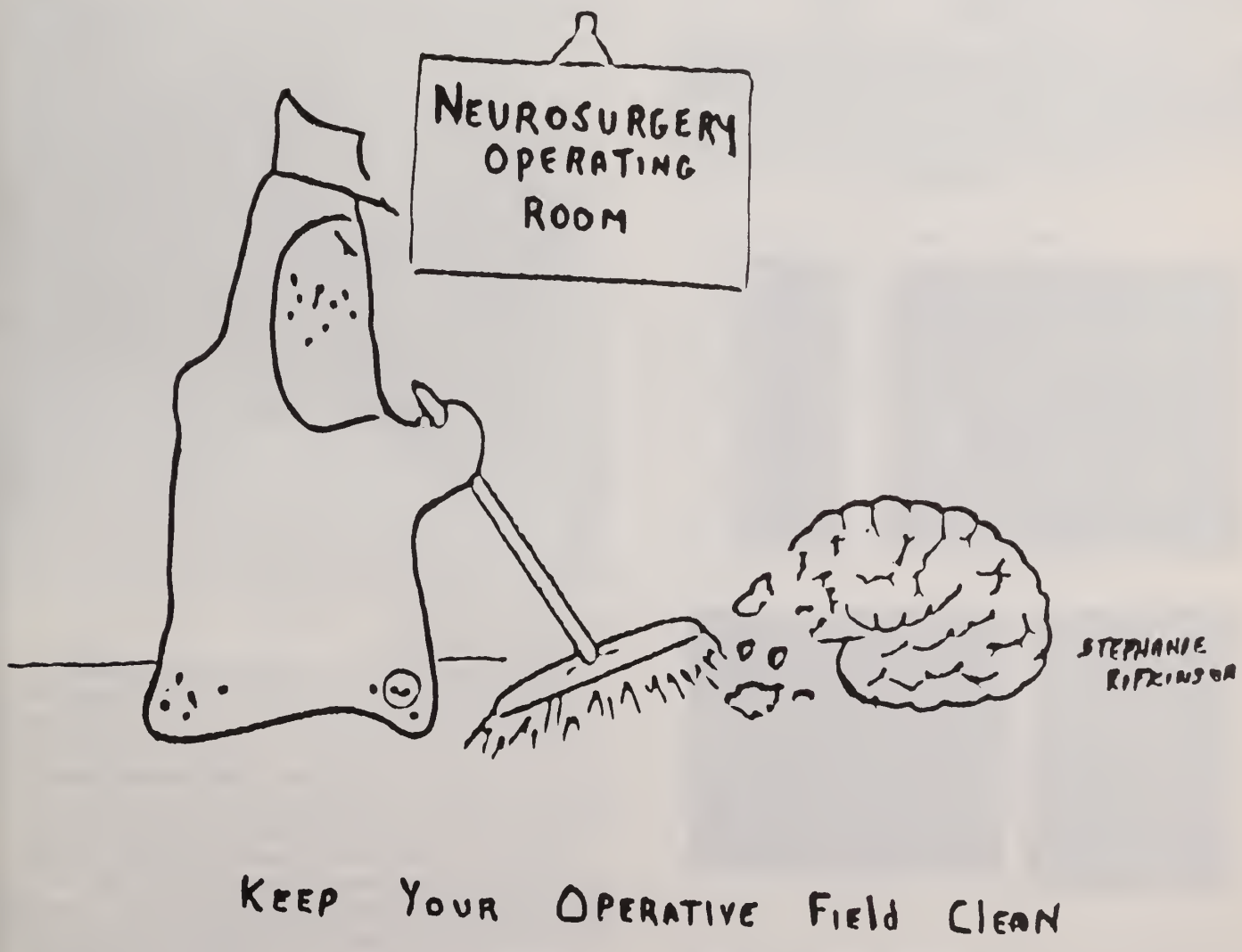
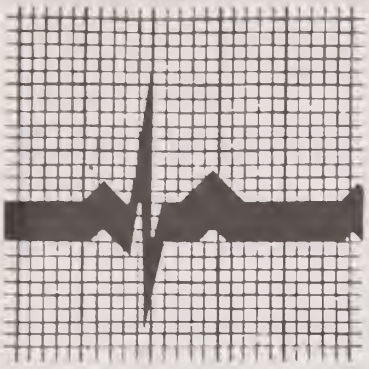
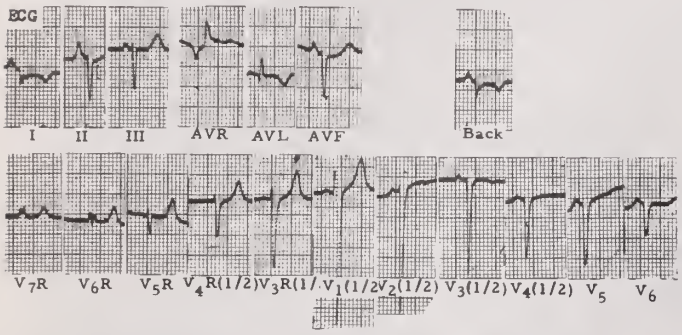


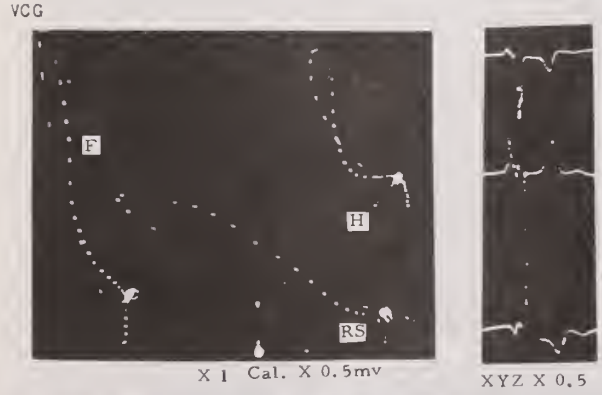


ELECTROCARDIOGRAM OF THE MONTH

Charles D. Johnson, MD

This 39-year-old male had a history of a heart murmur since age 12 years, and two previous hospital admissions for "meningitis". Chest pain and congestive heart failure occured. His last hospital admission was depicted by dyspnea, diarrhea, abdominal and left shoulder pain and neurological symptoms and signs (aphasia, flaccid paralysis, Babinski sign and clonus, rotating eyes, tremor and unconsciousness). There were a grade 3 systolic murmur over the precordium and a grade 2 diastolic murmur. Laboratory data: HB 17 gm. WBC 17500 with 94 segs, SGOT 65 units, LDH 670 units, glucose 35 mg percent, normal brain scan, EEG: slow activity, 21 red blood cells in the CSF, negative blood culture. Neurological deterioration progressed. Cardiorespiratory arrest transpired 8 days after admission. See Figures 1-4.





Questions

1. What specific diagnoses can be made from the electrocardiogram (ECG), vectorcardiogram (VCG) and roentgenograms?
2. What clinical and embryological diagnoses can be derived by deductive reasoning?
3. Discuss the differential diagnosis.
4. What complications have ensued?

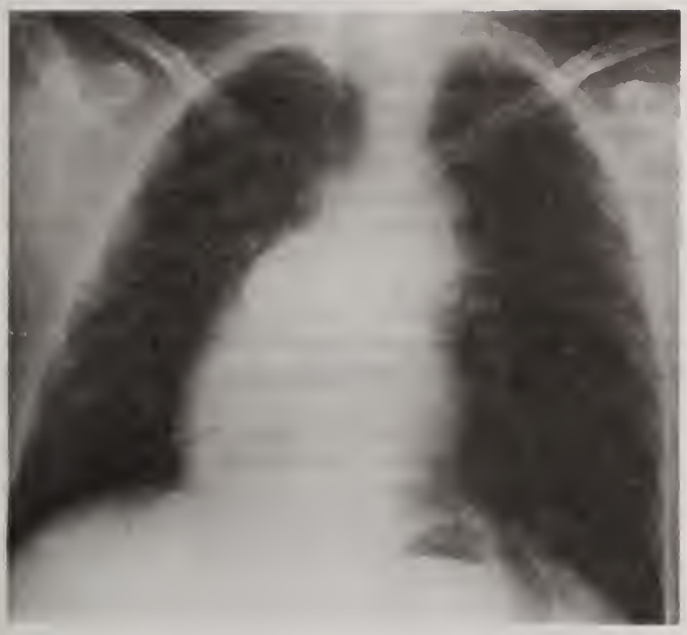
Answers: (autopsy)

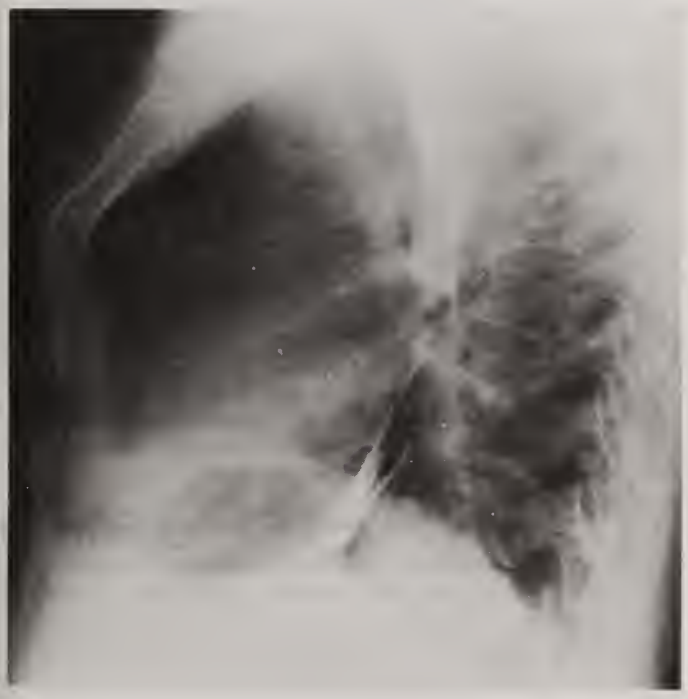
Cyanotic Congenital Heart Disease - clubbing, polycythemia.
Cardiac Malposition.
Dextroversion - S.D.S. or,
Dextroversion with Corrected Transposition of the Great Arteris (TGA) S, L, L
Pulmonic Stenosis (PS) - No valve cusps.
Ventricular Septal Defect (VSD). 3.5 x 2 cm. Reversed interventricular shunt.
Cardiomegaly 620 gm

Right ventricle (RV)	2 cm.
Left ventricle (LV)	2 cm. Concentric, severe
Right atrium (RA)	3 mm.
Left atrium (LA)	3 mm.

Abnormal origin and distribution of the coronary arteries.
Pulmonary arterial wall thickening and mural thromboses.
Encephalomalacia - multiple recent and old. Anoxic changes, focal hemorrhages, arterial mural thromboses, atrophy.
Massive vascular thrombosis of right lobe of liver.
Infarcts of spleen and kidneys.
Thoracid deformity, pectum carinatum and excavatum, scoliosis.

From the Department of Medicine, Section of Cadiology, UPR School of Medicine, Río Piedras, P.R.





ECG

P-R interval 0.12 sec. QRS axis + 240°. P wave upright in all leads (peaked in leads 1, 11, aVF) except a VR, V_6R, V_7R. QS complex in leads 1, V_4-$_6$, back; rS in leads 11, 111, a VF, V_3R, V_1-$_2$ (deep S), RR′ in V_7R. T waves inverted in leads 1, aVL, upright in right chest leads.

VCG

The QRS loops are located posteriorly, superiorly and rightward. The initial vector exists directly rightward. Afferent slowing is present.

RA and RV enlargement. Incomplete right bundle branch block (RBBB).

Roentgenogram

The aortic arch and stomach are located on the left side (probably the ascending and descending aorta also), while the apex and majority of the heart are rightward. The right hemidiaphragm is lower than the left. The bronchial anatomy appears normal for Situs Solitus (SS). The sternal deformity is evident on the lateral projection.

Discussion

Dextrocardia occurs as 1 case per 9000 persons, and in 2.7-5 percent of cases with congenital heart disease. Numerous types can be identified. SS exists in 33-50 percent of cases. In the past Tetralogy of Fallot was considered rare in dextrocardia, but other authorities have not found this to be true. The cardiac apex is usally projected over the lower hemidiaphragm.

Neurological complications occur in 25 percent of congenital heart disease patients. Spontaneous cerebrovascular accidents, thromboses and abscess are observed in 2-4 percent of cases. Cerebral infarctions are related to the polycythemia, increased blood viscosity and cerebral vascular resistance, decreased cerebral blood flow and hypoxia. Preexistent neurocirculatory damage is characteristic. The brain scan and EEG of the patient favored a thrombotic infarction over an abscess. Extracardiac anomalies are common in dextrocardia.

Differential Diagnosis

1. Simple PS and VSD in a SS heart, the dextrocardia due to marked RV enlargement. Existence questionable.

2. Dextroposition (Secondary dextrocardia).

The heart is shifted to the right because of extracardiac pulmonary, diaphragmatic or skeletal pathology - emphysema, agenesis of the right lung, pleural effusion, eventration or hernia of the diaphragm, thoracic cage deformities, etc. The ECG may be normal, show low voltage or be similar to that of dextroversion.

3. Mirrow-Image Dextrocardia with PS and VSD.

No Situs Inversus (SI). No inversion of heart chambers. Usually without associated defects. Incompatible ECG, X-ray, autopsy.

4. Anatomically Corrected Malposition (Ventricular Transportation). Rare. Abnormal spatial relationship between the great arteries which are also abnormally related to the ventricles, but the aorta (Ao) and pulmonary artery (PA) arise from anatomically appropriate (concordant) ventricles. The anterior descending coronary artery (ADCA) arises from the left coronary artery and has a normal distribution.

The diagnosis most likely is either Dextroversion or Dextroversion with Corrected TGA. There was dextrocardia (rightward apex, heart predominantly in the right chest) and SS. The trilobed lung and RA are located on the right following the liver and vena cava. The bilobed lung, aortic arch, LA and stomach are on the left. The positive P wave in lead 1 supports the rightward sinoatrial node and RA, atrial noninversion, as does the normal bronchial anatomy by the rule of viscero-atrial concordance. The anatomical RV appears to be rightward as ventricular noninversion, a concordant D-loop, from the QRS morphology of a R or rS complex over the right chest identifying the RV, and a q wave in a VL and WSs in leads V_{4}-$_{6}$ suggesting a leftward LV.

5. Dextroversion (Insolated Dextrocardia, Dextrorotation, Dextrotorsion, Pivotal Dextrocardia). Normally related Great Arteries. Left descending Ao and stomach and right apex, SS.

This comprises 18-47 percent of cardiac malpositions, 2.8 percent of cyanotic heart disease. Heart disease, predominantly complex cyanotic (PS, VSD, Single Ventricle, Corrected TGA - 28-67 percent), is present in 75-90 percent of cases. Rotational arrest occurs at 6-9 weeks and the ventricular loop fials to rotate leftward. The ventricular portion of the heart is rotated counter-clockwise (ccw) on the longitudinal axis and to the right, bringing the ventricles side-by-side or the LV anterior (and inferior) to the RV, the LA anterior to the RA and the septum perpendicular to the frontal (F) plane.

X-ray: the ascending Ao is to the right of the PA; the heart retains its peculiar appearance whether or not the film is reversed; the right heart border (RV) shows an abnormal convexity of bulge.

ECG. VCG.: P waves are upright (or -+) in leads 1, a VL (axis + 30°-100°) and left precordial leads. The QRS axis is inferior and leftward or slightly rightward; the initial vector is oriented rightward. Leads 1, aVL, aVF- qr, QR or QS with T inversion; deep Q in lead 11, 111; rS in aVR; the precordial ECG is displaced to the right with the transitional R/S in V_3R to V_2; R, R/S or rS in right chest and a qr in the left precordium. T wave positive in leads 111, aVR, V_{1}-$_{2}$, V_3R to V_6R.

With RV hypertrophy: rightward axis shift; prominent deeper W and smaller r in lead 1, dominant R in leads 111, aVF; V_5R, V_6R with reciprocal S waves in V_{5}-$_{6}$.

RBBB- adds rSR, rsR, rRs complex.

VCG: P loops are leftward and anterior or anterior with ccw frontal rotation; there are prominent QRS forces directed to the left, anterior and inferiorly; initial QRS vector to right; ccw H loop.

6. Dextroversion with Corrected TGA (Inverted Transportation, L-Transposition, Mixed Dextrocardia with Ventricular Inversion). Common in cardiac malpositions.

The pathological description in the case is not clear or complete but the PA was described as "posteriorly localized in relation to the Ao", which if referring to the great arteries embryological disposition at their origin would mean "TGA". yet, this was not diagnosed and normal intrinsic atrio-ventricular and ventriculo-arterial connections were indicated (no ventricular inversion or discordance). By virtue of the rotation in simple Dextroversion, the Ao becomes left and *anterior* to the PA, as the aortic root arises from the anteriorly positioned LV. In ventricular inversion the coronary arteries demonstrate an inverted or mirrow-image pattern. The ADCA usually arises from the right coronary artery (true left) which originates from the right coronary sinus and it crosses the righ-sided outflow tract to supply the LV. The left coronary artery (true right) arises from the left sinus and supplies the RV. The noncoronary sinus is anterior.

X-ray: The ascending Ao courses vertically upwards or forms a leftward convexity and bulges along the upper cardiac border; the vascular pedicle is wide; the right heart border (LV) is smooth, tapers gradually and is not overtly convex.

ECG: The P vector is normal with a positive P in leads 1, V_6, negative P in V_6R. Lead 1 shows a qR or qs with usually T inversion. Often a R/S complex is seen in v_1 and T waves are usually upright in all precordial leads. There is reversal of the expected lateral precordial q wave patterns (q in the right precordium but not in the left).

VCG: P loops are left and anterior or anterior, and ccw in the H and F planes. QRS loops are located rightward with a clockwise H loop. The early vector is anterior (or posterior) and slightly rightward. The T loop is right and anterior.

Suggested Reading

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(Interesed readers may write for a copy of additional references)

artículos especiales

DISCURSO PRONUNCIADO POR EL DR. JOSE MARTI NUÑEZ AL TOMAR POSESION COMO PRESIDENTE DE LA ASOCIACION MEDICA DE PUERTO RICO EL 14 DE NOVIEMBRE DE 1981

TENGO UNA PREOCUPACION

Una preocupación de que nos están robando nuestra profesión por descuido nuestro, y nosotros lo estamos permitiendo.

Esta Asociación es una entidad idónea para bregar con la constante erosión que estamos sintiendo de todos lados.

Primero: ¿estamos decididos a dirigir? o ¿haremos como aquel famoso general del Siglo 18, que miraba la dirección de las tropas para estar seguro que iba al frente?

Segundo: nosotros, los reconocidos líderes, tenemos la responsabilidad de decir las cosas tal como son; y esto no es una tarea fácil.

Hay una falta de dirección y un mal definido coraje que nos divide, nos deforma y nos hace atacar nuestras instituciones que hasta ahora eran tenidas como sagradas.

Pero nuestro problema es más profundo y tenemos que reconocerlo.

El sistema de cuidado de la salud se está usando ahora, como la frontera final y última para cambios sociales.

Lo que el pueblo decida en términos de servicios de salud logrará actitudes que hará de la medicina una utilidad pública, impondrá servicios mandatorios, controlará el desarrollo de las facilidades y en última instancia, apretará la cuerda de la eficiencia del médico para cuidar de su paciente.

Lo que el pueblo decida puede muy bien determinar si estamos dando un paso irreparable hacia un total estado de bienestar público.

Estas decisiones hechas públicas, seguramente políticas, determinarán si el futuro del cuidado de la salud se mire a la luz fría de la razón o la deslumbrante luz de un foco a una solución o crisis política.

Afortunadamente, o quizás desafortunadamente, el sistema del cuidado de la salud tiene la capacidad de costar infinitamente y puede absorber cada dólar que la sociedad pueda proveer.

Nuestros recursos, sin embargo, son claramente limitados y requieren decisiones serias, si queremos balancear los recursos con las necesidades.

El asunto de cambios en el sistema de servicios médicos es en realidad un dilema.

De un lado tenemos que nuestra sociedad ha determinado que el cuidado de la salud es un derecho, y cada vez cree más que el cuidado médico no debe ser determinado por los ingresos y las circunstancias personales, sino por los mismos niveles de asistencia médica.

De otro lado, nosotros sabemos cómo ejercer un estilo de medicina, que si se extiende indiscriminadamente, será más costosa que lo que la sociedad pueda pagar, y aún más costosa en cuanto al mejoramiento en servicios de salud que podamos justificar, aunque sean insuficientes.

Nuestro propósito como Asociación está en saber distinguir entre los datos de la ficción, logrando una base desde donde podamos hacer decisiones racionales, y permitiendo la implementación de programas responsables.

Obviamente esto no s fácil.

Todos sabemos que las cifras no mienten, pero desafortunadamente, existen los demagogos.

También sabemos del peligro de aceptar ideas ciegamente, sin la adecuada interpretación de su verdadero significado.

Ejemplo:

Si miramos solamente a las cifras de mortalidad, nunca nos fijamos que en los hospitales muere más gente que en ningún otro sitio.

De la misma forma, si usted quiere estar seguro de que no hay una bomba en el aeroplano en que vuela, lleve una, estadísticamente no hay oportunidad de que haya dos bombas en el mismo aeroplano.

Igualmente importante es:

¿Cómo recopilamos la información?

Miremos el estudio que se hizo en Estados Unidos por John Banker, de Stanford, para los casos de cirugía de los años en la década del 70. Nos habla de la cirugía innecesaria que se practicó, hasta que estudió a los médicos y a los

abogados, los que llamó "consumidores sofisticados de cuidado de salud" y encontró que hicieron uso de los cirujanos un 30 por ciento más que la población general.

Si no podemos confirmar nuestra información, o estar seguros de que nuestra interpretación es válida, entonces debemos excluírla de nuestras decisiones.

Más que nunca tenemos la necesidad de una consistencia sabia de nuestros informantes en cuestiones cruciales.

Y en eso podemos estar orgullosos.

Algunos datos nos han creado problemas.

Y es el hecho de que la buena medicina es elevada en costo, ésto ha violentado nuestras relaciones con otros segmentos de la sociedad, particularmente con el Gobierno.

Señalo el factor costo, o más bien, la necesidad de costos moderados, porque esto ha creado controversia.

Es el más grande factor en muchos de los cambios que actualmente están transformando la medicina en nuestra Isla.

El aumento de los costos y la necesidad de detenerlos es en gran medida, lo que está detrás de programas como rigurosa supervisión en los hospitales, para PSRO, para la compra de medicinas genéricas más baratas, sustitución de medicinas genéricas, para medicina preventiva más efectiva, para ésto y para aquéllo, etc.

De modo que si los cambios que tenemos por delante tienen que ser los correctos, nosotros y nuestra sociedad, tenemos que actuar sobre una base sólida de datos en los costos de salud, antes que ficciones ilusorias.

Tenemos un gran reto ante nuestra Asociación y Dios sabe que es grande.

Hay un gran número de distorsiones, evasiones y exageraciones evidentes en nuestra sociedad en relación al costo de los servicios de salud y cuidado médico.

Ejemplo: es que el cuidado de alta calidad es costoso, y es tiempo que los economistas, los expertos, los consumidores, los planificadores profesionales y los legisladores, así lo admitan.

Es también un dato, que las causas que contribuyen al aumento de costos en los servicios de salud, son mayormente abstractos, inevitables y fuera de nuestro control.

Ellos incluyen:

Fuertes presiones inflacionarios en general, por las que el Gobierno debe cargar una gran parte de culpa.

Desarrollos extraordinarios en recursos clínicos y tecnológicos.

Expansión de los beneficios a los programas ofrecidos por el Gobierno.

Muchos de estos datos vienen de los análisis del Gobierno Federal.

Consideremos el libro de HEW "Background Book of Medical Care Expenditures, Prices and Cost" publicado a fines del año 1975.

Comentando el rápido ascenso de los cargos de hospitales, que es la mayor parte del dólar médico, el libro llanamente expone el eje ascendente de dos factores principales:

Uno: El aumento en jornales y precios pagados por los hospitales para mantener el mismo nivel de servicios ante la inflación.

Dos: Los gastos en los servicios mejorados que incluyen el costo del personal necesario, más equipo especializado.

Este libro señala esto claramente y dice:

Cito:

"Las facilidades y servicios que eran inaccesibles dos décadas atrás, o que solamente sé usaban en hospitales de enseñanza altamente sofisticados, se ofrecen hoy en día en hospitales de la comunidad".

Dios nos dio salud y belleza. Lo que hacemos de nuestro cuerpo es nuestra responsabilidad.

Si todo, incluyendo nuestro compromiso social de que el bienestar es un problema de salud, que puede significar cualquier cosa desde la ansiedad sobre la caspa hasta el resentimiento de no ser invitado a una fiesta; si todas estas cosas son problemas de salud, entonces, no hay límite a los recursos que podemos sacrificar en el tratamiento; o la burocracia se verá tentada en regular el acceso a estos tratamientos. Lo importante es que la función del médico, al igual que el concepto de salud, es cada vez más amplio, no puede ni debe encajonarse en límites estrechos. Los médicos tenemos que asumir nuestra responsabilidad social cada vez mejor y la sociedad tiene que reconocer la misión profesional y social del médico.

Señores: el pueblo tendrá que establecer prioridades, ahora bien, ninguna legislación puede ser efectiva sin la buena voluntad de la clase médica, que tiene la disposición para ponerla a funcionar.

Este sencillo dato conlleva una gran responsabilidad.

No podemos darnos el lujo de la oposición sin tener las alternativas viables a los problemas claramente existentes.

No podemos hacer decisiones basadas en deseos o conveniencias.

Necesitamos reunir datos ciertos, interpretados racionalmente y luchar por los objetivos que nos dictan esos datos.

No necesitamos comprometernos con sectarismos, pero sí tenemos que hacerle frente a la realidad sin temor y con rectitud.

Solo actuando así, evitaremos caer en manos de los burócratas que demuestran poca tendencia a separar los datos de la ficción.

En esto es la Asociación Médica la organización que tiene la encomienda más importante de todas.

A todos los compañeros médicos les digo, que tienen que procurar la unidad de todos en los asuntos esenciales y al mismo tiempo darnos libertad en lo no esencial.

Nunca estaremos satisfechos, pero basados en datos objetivos, la Asociación Médica puede adoptar como su política las estrategias correctas y permitir a sus miembros libertad de táctica para ejecutar estas estrategias.

Como líderes podemos esperar operar con grandes dudas, pero si podemos conquistar esas dudas por medio de planificación, unidad y sabias decisiones, solo así podremos ser valiosos en la actualidad y en el futuro.

NOTA BIOGRAFICA

José Martí Núñez, MD - Presidente
Asociación Médica de Puerto Rico

El Dr. José Martí Núñez nació en el pueblo de Caguas, Puerto Rico, el 8 de noviembre de 1930. Hijo del Sr. José Martí Jiménez y la Sra. Rosario Núñez González. Tiene un hermano médico también, el Dr. Rafael Martí Núñez, quien ha ostentado el cargo de Senador por el Distrito de Caguas-Humacao hace dos cuatrenios.

Se educó desde el primer grado hasta cuarto año de Escuela Superior en el Colegio Católico de Caguas, graduándose en el 1949 con notas sobresalientes.

Prosiguió a hacer estudios de Pre-médica en la Universidad de Notre Dame en South Bend, Indiana, pasando luego a estudiar medicina en España. Estuvo en la Universidad de Madrid, Granada y Zaragoza, graduándose en el 1961.

Hizo su Internado en el Hospital Municipal de la Capital, previa aprobación del examen Educational Council for Foreign Medical Graduates (E.C.F.M.G.). Hizo dos años de especialización en Obstetricia y Ginecología en el Hospital Municipal de Río Piedras, trasladándose a Bridgeport Hospital en Bridgeport, Connectituc, donde terminó su especialidad, habiendo sido durante todo el año el Chief Resident del Departamento.

Tomó cursos de Post-Graduado durante ese año en la Universidad de Harvard.

Se trasladó a Puerto Rico, donde empezó a trabajar con el Gobierno de la Capital, brindándole sus servicios de la especialidad en varias de sus dependencias, como los Centros de Diagnóstico y Departamento de Obstetricia y Ginecología del Hospital Municipal del Centro Médico.

Una vez establecida su profesión en la cuidad de San Juan, se envolvió en los quehaceres de la Asociación Médica, en la cual ha pertenecido a varios Consejos de la Junta de Directores, ha sido Delegado de la Cámara de Delegados por muchos años, Presidente de varios Consejos de la Junta Directiva Central, Presidente del Distrito Este —siendo éste el más grande y poderoso Distrito de la Asociación Médica—, Presidente de la Cámara de Delegados de la Asociación Médica y en el 1980 fue electo al cargo de Presidente de la Asociación Médica, tomando posesión del cargo en noviembre de 1981 y actualmente preside esta organización.

Está casado desde hace 16 años con la Sra. Ivette Caloca Rojas de la ciudad de Río Piedras, y han procreado tres hijos, dos varones y una niña de 14, 11 y 9 años respectivamente. Estos cursan estudios en la American Military Academy, siendo estudiantes de altos honores, habiéndose ganado las medallas de excelencia académica en varias ocaciones.

Ha sido miembro de agrupaciones cívico-sociales en la Capital de Puerto Rico, tales como al Casino de Puerto Rico, la Casa de España, el Caparra Country Club y el Club de Leones de Garden Hills, donde le rindieron homenajes por su labor destacada.

Sus ocupaciones actuales dentro de la Asociación Médica y su profesión lo han retirado un poco de las actividades sociales.

Actualmente sigue trabajando para el Gobierno de la Capital, donde lleva 21 años y comparte su tiempo en la práctica privada de su profesión durante las tardes.

NEWS

CHICAGO — A physician from Sañ Juan, Puerto Rico, has been named the 1981 recipient of the Gold Key Award of the American Congress of Rehabilitation Medicine (ACRM) for meritorious service to the cause of persons with physical disabilities.

He is Herman J. Flax, MD, 64, who has been chief of the Physical Medicine and Rehabilitation Service at the Veterans Administration Hospital in San Juan for the past 30 years.

A former president of ACRM, Dr. Flax was honored with the Gold Key particularly for his work in establishing residency training programs in physical medicine and rehabilitation (PM&R) at the San Juan VA Hospital in 1957 and at the University of Puerto Rico Medical Sciences Campus in 1964. Physicians who specialize in PM&R are called "physiatrists", and the majority of the 75 physiatrists practicing in Puerto Rico today were trained in the programs that Dr. Flax was instrumental in establishing.

A native of Richmond, Virginia, Dr. Flax is currently president-elect of the International Rehabilitation Medicine Association, which will hold its Fourth World Congress in San Juan next April.

Dr. flax earned his medical degree at the Medical College of Virginia in 1940. After serving with the U.S. Army Medical Corps, he was director of public charities in Manatí, P.R., from 1941 through 1944, then joined Puerto Rico's State Insurance Fund as a medical inspector and later as director of the Fund's Department of PM&R.

He joined the San Juan Veterans Administration Hospital staff in 1951 as acting chief of the Physical Medicine and Rehabilitation Service and was subsequently appointed chief of service. A diplomate of the American Board of PM&R (1951), Dr. Flax joined the faculty of the University of Puerto Rico School of Medicine in 1952 as assitant clinical professor and remains on the faculty today as a full professor.

Dr. Flax has been president of the Section of Physical Medicine and Rehabilitation of the Puerto Rico Medical Association on two occasions. he has published more than 70 scientific papers on many facets of PM&R, and has been an untiring spokesman for the field of physical medicine and rehabilitation.

The American Congress of Rehabilitation Medicine is a national organization of aproximately 2,600 specialists in various professions dedicated to helping persons with physical disabilities realize their fullest potential for independent living and self sufficiency.

The Gold Key will be presented to Dr. Flax at an awards luncheon to be held in conjunction with the organization's 58th Annual Scientific Session in San Diego, November 1-6. The luncheon is Tuesday, November 3.

TOXIC SHOCK SYNDROME PROBABLY MORE FREQUENT THAN BELIEVED

CHICAGO — Toxic shock syndrome occurs more commonly than is currently recognized, claim two Minnesota physicians, and doctors may miss some of these cases if they adhere to closely to criteria for diagnosis of the syndrome established by the centers for Disease Control (CDC).

Writing in the Journal of the American Medical Association (Nov. 13), Robert W. Tofte, MD, and David N. Williams, MB, ChB, report the cases of 17 women who presented with definite or probable syndrome. The seven women described as having probable syndrome did not demonstrate symptoms that satisfied all the current strict CDC criteria.

These criteria are 1) temperature of 102° F, or above; 2) rash with subsequent peeling; 3) low blood pressure; or dizziness, fainting or decrease in blood pressure; or dizziness, fainting or decrease in blood pressure upon standing up; 4) clinical or laboratory abnormalities in three or more organ systems; and 5) reasonable evidence for the absence of other causes.

The authors found that their patients presented with a broad spectrum of clincial signs and symptoms. No single sign, symptom, or laboratory test abnormality, or combination however was presented in every case, and no patient had involvement of all organ systems.

An initial diagnosis of syndrome was suspected in only seven patients, the remaining ten were treated at first for such condictions as gastroenteritis, urinary tract infection, and Rocky Mountain spotted fever.

It has been recognized that most women with the syndrome become ill during menstruation and that the risk of the syndrome developing is significantly greater is women who use tampons than in women who use other types of protection. Physicians currently believe tha poisons formed by th bacterium *Staphylococcus aureus* are responisble for causing the symptoms of the syndrome. Some persons may be more susceptible to these poisons than others, accounting in part for the wide variety of symptoms that seem to result.

Unless the diagnosis of the syndrome can be excluded with certainty, the authors advise, any women with a fever of unknown origin that occurs during menstruation, is recurrent, or is associated with a rash should be suspected of having the syndrome, even if certain criteria for definite syndrome are absent. It would be prudent, they add, to begin treatment with an effective anti-staphylococcal antibiotic.

MORE AGGRESSIVE TREATMENT URGED FOR PATIENTS WITH PROSTATE CANCER

CHICAGO — A large number of men with prostate cancer that has not spread beyond the original tumor site should be receiving curative radiation therapy or surgery, but aren't, according to the American College of Surgeons and the American College of Radiology.

A Medical News report in the Journal of the American Medical Association (Oct. 16) states tha findings from a 1979 ACS survey show that most of these patients are receiving either no treatment at all or treatments that offer relief from symptoms and slow the progress of the tumor but do not attempt a cure. These palliative measures include removing part of the enlarged prostate to relieve urine retention, estrogen therapy, and removal of one or both testes.

More aggressive treatments, such as radiation therapy and removal of the entire prostate gland, are not being attempted as often as they should, say spokesmen for the two specialty groups.

One possible reason for the lack of aggressve therapy is that patients seem to do well without it. ACS figures indicate that, regardless of the type of treatment received, 75 percent of patients with the least serious stage of the disease are alive five years after diagnosis. Among patients with the most serious sage of the disease, 50 percent are alive after five years.

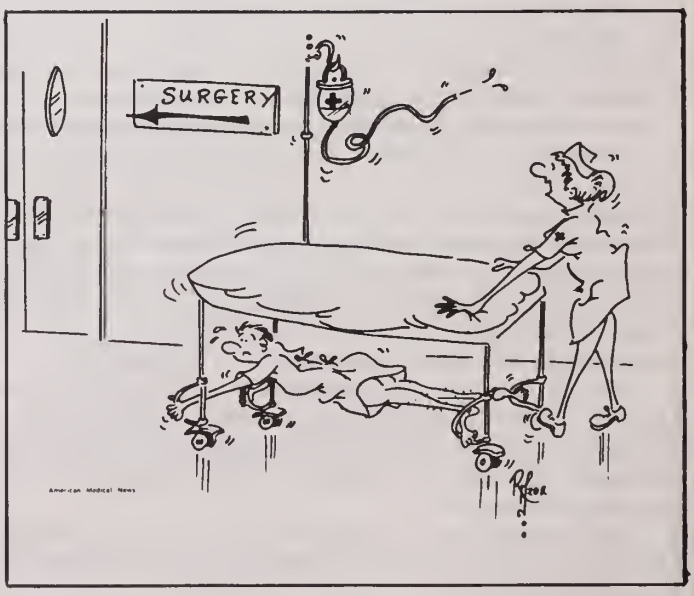
Side effects may be another reason for avoiding more curative treatment. Surgery is almost always followed by impotence and in 10 to 15 percent of cases by incontinence. Impotence follows radiation therapy in about 30 to 40 percent of cases.

In addition, most physicians think of prostate cancer as a slow-growing malignancy that occurs primarily in elderly men. They feel they must weigh the risks and side effects of radiation and surgery against the limited number of years naturally remaining to their patients.

Most men are living longer, however, so prostate cancer deaths are increasing, according to Gerald P. Murphy, M.D., director of Roswell Park Memorial Institute, Buffalo, N.Y. For that reason, physicians should think about treating the disease more aggressively, he says.

Radiologists contend that radiation therapy is the prime treatment for prostate cancer. They cite a higher survival rate after three years as compared with surgery, lower incidence of associated illness, and lower cost when compared to surgery.

Surgeons feel that more long-term studies-up to 10 or 15 years-are needed before a significant comparison of survival rates can be made.



Reprinted from American Medical News. April 2, 1982

CARTAS AL EDITOR

PREGNANCY IN WOMEN OVER 40 YEARS OLD

It was observed that pregnant women ages 40 and over had contributed significantly to our perinatal mortality and maternal morbidity. In order to assess this, a retrospective analysis was undertaken of pregnancies in women ages 40 and over, over a three year period January 1977 to January 1980. During this period there were a total of 9,960 deliveries at this hospital. Lincoln Hospital serves an indigent population in the lower socio-economic area of the South Bronx in New York City with a population of primarily Hispanic (68 percent) and Black patients (20 percent).

An analysis was performed for pregnancy outcomes in this group of patients age 40 and over at the time of delivery. We compared the results of the pregnancies with a similar number of randomly selected patients ages 17-39.

The total number of patients in this group of women 40 and over was 115. This represents 1.06 percent of the total number of patients delivered at this hospital during these three years. The maternal ages this group ranged from 40 -45 years. More than half of these patients were grand multiparas, paras 5 and over. Of the 115 woman, 25 percent in the control group. Because of lack of prenatal care, patient refusal as well as late arrival to clinic, only 13 percent of these patients had genetic counseling and amniocentesis.

Medial complications were higher in this group of woman as compared to the controls. In particular the incidence of diabetes was three times higher than controls or 19.3 percent versus 6 percent. Similarly, hypertensive disorders were also three times higher - 22.8 percent as compared to 7.8 percent in control.

Intrapartum complications like meconium staining of amniotic fluid was 13 percent as compared to 7 percent in the controls, while premature rupture of membranes was 15 percent versus 7 percent. Placenta previa and abruptic placenta were twice as high as in the control group: 2.6 percent versus 1 percent. As would be expected of these antepartum and intrapartum complications, the cesarean section rate was more than double in the study group-31.3 percent versus 14.2 percent in controls. Although there was no maternal deaths in these women the incidence of postpartum hemorrhage, endometritis, wound infection and need for blood transfusion was higher.

Perinatal Data

There were no infants with Down's Syndrome but nine babies were born with congenital malformations. Of these, five were major and the remainder minor —(an incidence of 7 percent as compared to 2 percent in the control group). The stillbirth rate was 4.2 percent compared to 1 percent in the controls. There was no significant difference in the neonatal death rate between these two groups. However, prematurity was 1 1/2 times than in the control group (17 percent versus 12 percent). These women had 38 percent small for gestational age babies as compared to 19 percent of the controls. The overall perinatal mortality was 50.8/1,000 live births as compared to 18/1,000 in the control.

Of the 115 females in the sample 30 had surgical sterilization. Ten chose an alternative form of contraception while 75 patients refused any form of birth control.

It seems from this analysis that women over 40 run a 2 to 4 fold increase of medical complications. Of these, diabetes and hypertension occur three times as frequently as in younger age group and perinatal mortality is increased three fold.

We feel that this group of women age 40 and above should have individualized antepartum and postpartum counseling. This is a small group of patients, yet they have major medical and social problems. A team approach with obstetricians, social workers, family planning counselors, and geneticists would definitely improve the outcome in these women and lower the perinatal morbidity and mortality.

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CAUSAS DE INFERTILIDAD EN UNA PRACTICA PRIVADA

Con la escasez de niños para adopción debido a la liberación legal del aborto inducido ha hecho crisis el problema de infertilidad tanto en Estados Unidos como en Puerto Rico.

No existen en Puerto Rico estadísticas sobre el problema de infertilidad en nuestra población. Esto me ha movido a estudiar las causas de infertilidad entre mis pacientes privados.

Hay otros ginecólogos que también están interesados en este aspecto de nuestra especialidad y pueden ellos con sus experiencias ayudar a poner en perspectiva correcta esta situación.

Para bailar el tango se necesitan dos, lo mismo para que ocurra un embarazo. Las condiciones esenciales para que ocurra un embarazo son las siguientes:

1. Oogénesis y espermatogénesis normales.
2. Conductos abiertos y patentes.
3. Coitus durante el tiempo fértil de ovulación.
4. Inseminación normal.
5. Preparación adecuada del endometrio para que se logre la implantación y se mantenga.

Son estos factores los que han llevado a desarrollar un programa básico de investigar dónde radica el problema en y entre los cónyugues.

En el historial de la mujer se le da importancia a la 3 M: historial menstrual, marital y materno. En el examen físico se busca si hay contraindicación a un embarazo y si pueden surgir complicaciones.

Se procede luego con la investigación de las causas de infertilidad acordándose siempre de Primum Nonnocere:

a) Ovulación y espermatogénesis:
Ovulación se determina con temperatura basa, con biopsia del endometrio en el día 22 del ciclo y/o con determinación de progesterona en plasma en el día 22 del ciclo.
Espermatogénesis se determina con un análisis de semen, obteniendo el semen luego de 3 a 5 días de abstinencia. Se debe repetir el análisis de semen 2 ó 3 veces.

b) Conductos abiertos y patentes:
En la mujer se determina con insuflación (Rubins), hysterosalpingograma y/o chromo-perturbación. Estos procedimientos se llevan a cabo después de la menstruación pero antes de la ovulación alrededor del 10mo. día del ciclo menstrual. En el hombre la presencia de espermatozoa indica que el vas está patente.

c) Coitus al tiempo fértil se determina con la gráfica de temperatura basal.

d) Inseminación normal se determina con la prueba post-coital, de 2 a 8 horas después del coito. Se obtiene moco del cuello y se examina para la presencia de espermatozoas y moviéndose.

e) La preparación del endometrio se determina con una biopsia del endometrio en el día 22 del ciclo y debe ser leída por un patólogo que conozca los criterios de Noyes y Hertiz para fijarle fecha al endometrio.

Hay otras pruebas que pueden ser utilizadas en la evaluación de infertilidad como:

Prolactina - se debe determinar cuando se encuentra galactorrhea, amenorrheas de más de 3 meses, cuando no se consigue ovulación con clomid.

Laparoscopía - indicada en casos de infertilidad no explicada, y cuando se considera cirugía reconstructiva de tubos.

Pruebas inmunológicas cuando la prueba post-coital revela espermatozoas que no se mueven, teniendo el esposo un análisis de semen adecuado.

Pruebas de tiroide, cortisol, 17 OH progesterona, tolerancia de azúcar según indicadas.

Los resultados obtenidos fueron los siguientes: se estudiaron 190 matrimonios de los cuales 27 (14 - 2 porciento) no completaron la evaluación.

De los 163 restantes las causas que se encontraron:

1. Esposo 30 (18.3 por ciento)
2. Esposa 69 (42.3 por ciento)
   - a) Cervical 1
   - b) Luteal 10
   - c) Ovulación 18
   - d) Tubo 36
   - e) Endometriosis 4
   - f) Sin explicación 8 (4.9 por ciento)

Múltiples causas 56 -(34.3 por ciento)

Analizando en esta forma hay más problemas con la mujer que con el hombre. Y como causa hay un grupo considerable en que las causas son múltiples.

Al analizar el grupo de causas múltiples encontramos:

1. Esposo y esposa	35
2. Esposa sola	21
3. Ovulación y esposo	10
4. Tubo y esposo	14
5. Tubo-ovulación y esposo	3
6. Luteal y esposo	8
7. Tubo y ovulación	16
8. Tubo y luteal	4
9. Cervical-tubo y luteal	1

Al agruparlos todos encontramos esposo 30 (sólo) 35 en causas múltiples para un total de 65.

Esposa sola 69 - 35 en causas múltiples - 21 en causas múltiples de ella sola hacen un total de - 125. Así que también vemos que el problema es mayor en la mujer. Y al analizar las de la mujer encontramos:

1. Cervical	2
2. Luteal	23
3. Ovulación	47
4. Tubo	74
5. Endometriosis	4

De nuevo los problemas de tubo los más comunes. Al analizar las causas de infertilidad en nuestra práctica encontramos que un 14.2 por ciento de las parejas no terminan la evaluación.

La incidencia de infertilidad no explicada es de 4.5 por ciento. El problema es más de la mujer, y las dos causas principales son problemas de tubo y ovulación. El hombre como problema solo es responsable de un 18.3 por ciento de los casos. Hay un 34.3 por ciento de casos en que las causas son múltiples.

Edward O'Neill, MD
San Juan, P.R.

abstractos de la literatura médica

SURAL NERVE BIOPSY IN SYSTEMIC NECROTIZING VASCULITIS

Wels, S.J., Sunwood, I.N. and Joong, S. From University of Alabama, Birmingham, Alabama. American Journal of Medicine 71: 525-532, October 1981.

This study of 17 patients with vasculitic neuropathy (polyarteritis nodosa in 11, rheumatoid arthritis in five, and systemic lupus erythematosus in one) revealed the following: (1) Polyneuropathy is the most common manifestation of peripheral neuropathy in polyarteritis nodosa; (2) Peripheral neuropathy is more common in systemic necrotizing vasculitis than physical examination alone suggests. Adequate electrophysiologic tests can detect asymptomatic peripheral neuropathy in a substantial number of patients; (3) Abnormal sural nerve conduction is a prerequisite to the demonstration of vasculitis on biopsy of this nerve. Thus, in using abnormal sural nerve conduction as a guide in nerve biopsy, the diagnostic yield of sural nerve biopsy will be greatly enhanced.

(Submitted by Edwin Mejías, MD, VAH)

EFECTOS DEL VERAPAMIL EN LA TAQUICARDIA SUPRAVENTRICULAR EN NIÑOS

Porter, J.C., Gillette, P.C., Garson, A., et al. Am J. Cardiol. 48: 487, Sept. 1981.

El verapamil es un agente antiarrítmico extensamente usado en ocho países y recientemente aprobado para su uso en los Estados Unidos de América. Ejerce su efecto como antagonista del calcio a nivel celular y también deprime la función del nodo atrioventricular (A-V) al prolongar su período refractario.

Se le administró el verapamil a 13 pacientes con taquicardia supraventricular (TSV) recurrente. Las edades fluctuaron entre 6 semanas y 16 años. El mecanismo de la TSV había sido determinado por estudios electrofisiológicos invasivos en todos los casos. Estos eran: a) reentrada nodal A-V, b) reentrada por tracto accesorio, c) automatismo atrial ectópico, d) automatismo ectópico a nivel de la unión ("junctional").

El verapamil endovenoso (1V) logró suprimir la TSV en todos los pacientes cuyo mecanismo era por reentrada, ya bien fuese a nivel del nodo A-V, o por un tracto accesorio. Fue parcial o totalmente inefectivo en el resto. En los casos con TSV por atuomatismo a nivel de la unión ("junctional") se produjo hipotensión severa.

El medicamento por vía oral fue efectivo solamente en aquellos casos en que su administración IV logró abolir la TSV y evitarla luego de la estimulación de prematuros atriales.

Los autores señalan que en los pacientes pediátricos la efectividad mayor del verapamil es convirtiendo aquellas TSV por reentrada cuyo mecanismo depende de la conducción nodal.

Se concluye que el verapamil es efectivo en la edad pediátrica dependiendo del mecanismo de la TSV y que éste debe siempre conocerse antes de comenzar la terapia. Se advierte que los efectos a largo plazo en niños no son bien conocidos y que requieren investigación a fondo.

(Sometido por Rafael Villavicencio, MD)

LYMPHEDEMA INCIDENCE AFTER SPECIFIC POST-MASTECTOMY THERAPY

Markowski, J., Wilcox, Helen, P.A. - Arch. Phys. Med. Rehab. 62: 449-452, 1981.

En un estudio retrospectivo, la incidencia de linfedema fue analizada en 58 mujeres entre las edades de 35-81 que habían recibido un programa de tratamiento específico después de una radical o modificada radical mastectomía debido a carcinoma de mamas en el hospital del Condado. El 39 por ciento (23 pacientes) tuvieron tratamiento de cobalto y el 48 por ciento (28 pacientes) tuvieron cicatrización tardía de la herida. Medidas circunferenciales de las dos extremidades superiores habían obtenido respuesta específica en el sitio. Al final de 12 meses, 69 por ciento de los pacientes no tenían linfaedema; 22.4 por ciento tenía linfaedema mínimo; el 5.2 por ciento tenía linfaedema severo. El beneficio de un seguimiento cercano y tratamiento específico de los pacientes mastectomizados son evidencia en este estudio por un relativo grupo grande de pacientes que permanecieron libres de linfaedema por un período extendido de tiempo en cuanto a las complicaciones de la cicatrización de las heridas.

(Sometido por Edgar Baucage, MD)

LOWER EXTREMITY FRACTURES AFTER SPINAL CORD INJURY: A RETROSPECTIVE STUDY

Ragnarsson, K.T., Sell, G.H. - Arch Phys Med Rehab 62: 418-423, 1981.

Las fracturas en extremidades inferiores, luego de lesión al cordón espinal, son más comunes en pacientes paraplégicos que en los cuadriplégicos, probablemente debido a un mayor nivel de actividad. La mayoría de las fracturas son patológicas, en huesos con osteoporosis, y ocurren sin ser ocasionadas por trauma o son ocasionadas por un trauma leve. Las fracturas supracondilares y del

hueso del fémur son las más comunes. Aunque la formación de callo es usualmente rápida, el proceso de cicatrización de la fractura puede demorarse. El principal objetivo en el manejo del paciente, que es mantener la independencia funcional y sin complicaciones, se obtiene con un manejo no quirúrgico que consiste de tracción o poner un yeso bien acojinado seguido de la movilización temprana de la coyuntura.

(Sometido por Josefina Padró Ramírez, MD)

MYOFASCIAL TRIGGER POINT SYNDROMES IN THE PRACTICE OF RHEUMATOLOGY

Reynolds, MD - Arch Phys Med Rehab 62: 111-114, 1981.

El dolor referido de un músculo puede enmascarar el dolor procedente de una articulación o dolor de tipo radicular asociado a enfermedad de las articulaciones espinales, llevando a errores en el diagnóstico y tratamiento. Cuando existe enfermedad articular, ésta predispone a los síndromes de puntos de gatillo miofaciales ("trigger points"). Con la artritis, los puntos de gatillo musculares son el resultado de una mobilidad disminuída con acortamiento prolongado de los músculos, de fuerzas mecánicas anormales sobre los músculos y de estímulos procedentes de articulacioens enfermas. Durante el examen para signos de desórdenes miofaciales, el número de puntos dolorosos en mujeres con artritis reumatoidea era el doble que los encontrados en mujeres sin enfermedades reumatológicas. Es importante considerar esta alta frecuencia de síndromes miofaciales en personas con artritis cuando tratamos dolor o debilidad, las cuales podrían deberse a músculos en vez de a articulaciones. De otro modo, se ha propuesto sobre bases teóricas y clínicas, que los puntos de gatillo miofaciales pueden ocasionar enfermedad articular. Esta hipótesis tiene importantes implicaciones para el tratamiento de artritis.

(Sometido por Miguel Berríos, MD)

TARSAL-TUNNEL SYNDROME IN RHEUMATOID ARTHRITIS

Grabois, M., Puentes, J., Lidsky, M. - Arch Phys Med Rehab 62: 401-403, 1981.

Informes recientes sugieren una aumentada incidencia para la población general del síndrome del túnel tarsal en artritis reumatoidea, similar a lo previamente informado para el síndrome del túnel carpal. Sería importante probar esta suposición para el diagnóstico y manejo del dolor de los pies en pacientes con artritis reumatoidea. Treinta y nueve (39) pacientes con un diagnóstico clásico de artritis reumatoidea por criterios clínicos y de laboratorio se sometieron a estudios electrodiagnósticos en ambos nervios tibiales posteriores. Estas pruebas encontraron una incidencia de 15 por ciento de neuropatía periférica y del 5 por ciento para el síndrome del túnel tarsal en pacientes con artritis reumatoidea.

(Sometido por Miguel Berríos, MD)

ROCKER SHOE AS A WALKING AID IN MULTIPLE SCLEROSIS

Perry, J., MD - Arch Phys Med Rehab 62:59-65, 1981.

El potencial terapéutico de los zapatos daneses fue un hgallazgo incidental de Dorothy Clawson, paciente con esclerosis múltiple. La paciente era dependiente de muletas cuando ella trató un par de zapatos de un amigo y notó que la suela contorneada de éstos le permitieron pararse en posición erecta.

Luego de muchas pruebas y un análisis profundo, se formularon algunas reglas, modificaciones a los zapatos y técnicas para el entrenamiento en el caminar. La evaluación de los zapatos mecedores como una ayuda para caminar en los pacientes con esclerosis múltiple incluye un análisis mecánico del zapato, establecer cirterios clínicos para la selección apropiada de pacientes con los zapatos mecedores y sin ellos. Los pacientes que se han beneficiado ham demostrado que las medidas más importantes son que el punto mecedor (comienzo de la curvatura de la suela) debe de estar 1.5a 2cm. proximal a la cabeza del primera metatarso. Esto deja un pequeño espacio entre la cabeza del metatarso y el piso para iniciar la acción mecedora del antepie. El ajuste adecuado en el pie, además de correas en el talón, es necesario para mantener el pie en el zapato y que se pueda el paciente beneficiar de la asistencia mecánica del zapato consistentemente. Los zapatos mecedores fueron efectivos solo en pacientes que todavía tenían la habilidad de caminar independientemente y también tenían adecuada fuerza en cadera y pantorrilla, lo cual determinó era factor crítico. Los zapatos mecedores pueden reemplzar la mobilidad perdida del pie, tobillo, cuando la flexión plantar no exceda 15° y el paciente tiene suficiente fuerza en los músculos extensos para controlar el momentum creado. El mejoramiento de la marcha con los zapatos mecedores fue el ahorro en el costo neto de energía. Un promedio de 150 por ciento de la energía normal se gana con este tipo de zapato.

(Sometido por Tomás U. Poventud, MD)

SEXUAL PROBLEMS OF WOMEN WITH RHEUMATOID ARTHRITIS

Yoshino, S., Uchida, S. - Arch Phys Med Rehab 62: 122-123, 1981.

Un cuestionario referido a problemas sexuales se le ofreció a 112 féminas con artritis reumatoidea. Se recogieron las respuestas de 91 (81 por ciento). Los resultados indicaron: (1) las pacientes casadas recientemente estaban preocupadas por el embarazo; (2) el deseo sexual de la mayoría de las pacientes disminuyó, las relaciones sexuales fueron menos frecuentes y con menor satisfacción; (3) las articulaciones de la cadera y rodilla afectadas hacían difícil adoptar las posiciones para las relaciones sexuales; y (4) las pacientes que tenían relaciones sexuales insatisfactorias reportaron una demanda disminuída en llegar a orgasmos. Para conseguir una vida marital satisfactoria, las pacientes con artritis reumatoidea deben aconsejarse para que adopten una actitud positiva hacia la relación sexual con sus esposos.

(Sometido por M. Berríos, MD)

POLY-UNSATURATED FATTY ACIDS IN TREATMENT OF ACUTE REMITTING MULTIPLE SCLEROSIS

Dr. Bates and others - British Medical Journal, 1948, 6149: 1390-1391.

En un estudio controlado en relación con tratamiento a base de ácidos grasos poli no-ssaturados; en 116 pacientes (36 hombres y 80 mujeres) que padecían en 4 grupos. Dos grupos recibieron ácido linoleico: uno conjuntamente con la comida y al otro se le añadía en cápsula (Navdivelle) que contenía ácido linoleico gamma. Otros dos grupos de control: un grupo recibía ácido oléico en las comidas y el otro en cápsulas. El deterioro clínico y la frecuencia de los ataques no fue muy significativo entre los tratados y los no tratados. Se encontró que las exacerbaciones fueron más cortas y menos severas en pacientes que recibían una dosis alta de ácido linoleico que en los controles; pero en los que recibían las cápsulas (navdivelle) no había diferencia. Los resultados indicaron que suplementando la dieta con 20 gramos de ácido linoleico se afectaba la duración y severidad de remitencia de la enfermedad (Esclerosis Múltiple); pero no tenía ningún efecto en amortiguar el deterioro físico del paciente. La dosis de Navdeville no probó ninguna relación en la diea y la enfermedad.

(Sometido por Rafael Aguayo, MD)

CENTRAL NERVOUS SYSTEM LESIONS: SPROUTING AND UNMASKING IN REHABILITATION

Bach -y- Rita, P. - Arch Phys Med Rehabil 62: 413-417, 1981.

La recuperación de la función después de una lesión del Sistema Nervioso Central puede continuarse por meses o años después del trauma. Hya evidencia experimental considerable que concluye que la plasticidad del cerebro es de importancia para la recuperación funcional. Dos de los mecanismos de neuro-plasticidad considerados particularmente como causales son: 1. germinación colateral de células intactas hacia una región denervada después que sus aferentes han sido parcial o totalmente destruídos; 2. descubrimiento de vías nerviosas y sinapsis, las cuales no se usan normalmente para la función particular que se está estudiando pero que puede evocarse cuando el sistema dominante falla. El proceso de "unmasking" se discute extensamente en el contexto del papel de la rehabilitación en obtener recuperación máxima de la función.

(Sometido por Miguel Berríos, MD)

MOVIMIENTO EN LA ESPINA LUMBAR DURANTE EJERCICIOS DE LAS EXTREMIDADES SUPERIORES. UN ESTUDIO RADIOLOGICO EN PACIENTE PARA- Y TETRAPLEGICOS

Hein-Sorensen, O y Irstem, L. - Scand. J., Rehab Med 11: 13-27, 1979.

Los ejercicios de fortalecimiento durante el tratamiento de pacientes con fracturas lumbrares inestables producen un movimiento cifótico o lordótico sagital en la espina lumbar. Estos movimientos se han medido radiológicamente. Ejercicios de flexión de 45° en las articulaciones de los hombros causan un movimiento cifótico; mientras que la flexión a 110° y ejercicios de abducción a 90° producen un movimiento lordótico. La flexión de las caderas y rodillas a 45° producen un movimiento cifótico que se añade a los movimientos causados por los ejercicios de los hombros. El aumento en el peso de las estremidades superiores produce un aumento de todos los movimientos.

(Sometido por Rafael Aguayo, MD)

"GUIDELINES FOR THE DETERMINATION OF DEATH" PUBLISHED IN JAMA

CHICAGO — "Guidelines for the Determination of Death," part of a report from the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, has been published in the Journal of the American Medical Association (Nov. 13).

The Document is a summary of currently accepted medical practices for the determination of death, both cardiorespiratory and neurological (brain death).

The criteria were developed by more than 50 physicians form the fields of neurology, neurosurgery, electro-encephalogphy, critical care medicine, anesthesiology, and legal medicine. Taking into consideration new technologies in the laboratory confirmation of the diagnosis of death, they are the first update of standards for brain death since 1968.

The criteria are divided into two sections:

A. An individual with irreversible cessation of circulatory and respiratory functions is dead.

B. An individual with irreversible cessation of all functions of the entire brain, including the brainstem, is dead.

Each section is supplemented by an explanation of medical practices which may be used in determining cessation of functions and irreversibility, both of which must be demonstrated for a diagnosis of death. An individual presenting the findings in *either* section A *or* B is dead.

Of particular interest in the report is a discussion of medical conditions which can complicate the application of the neurological criteria. For example, drug intoxication, total paralysis and certain coma states can simulate death both in appearance and on some diagnostic tests.

In addition, the neurological criteria may not be reliable in cases involving hupothermia (body temperature less than 90° F). Hypothermia can mimic death while protecting the body against neurological damage by enabling the brain to survive with less oxygen.

The report also warns physicians to be cautious in applying the neurological criteria in the presence of shock and in children younger than 5 years.

The "Guidelines for the Determination of Death" were developed to help implement the Uniform Determination of Death Act, a model statue intended to end th confusion caused by laws differing from state to state. The statute was drafted by the American Bar Association, the American Medical Association, the National Conference of Commissioners on Uniform State Laws, and the President's Commission. To date, four states have adopted the statute: Vermont, Mississippi, Idaho and Colorado. At this time, the statute awaits signature by the Major of the District of Columbia.

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Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

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Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

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Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al mejor entendimiento del manuscrito.

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Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurement should be used preferentially).

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An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

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Reference: 1. Finnerty, F.A., Jr.: Hypertension: The Continuing Challenge, Scientific Exhibit, Meeting of the AAFP, Boston, Mass., Sept. 20-23, 1976.

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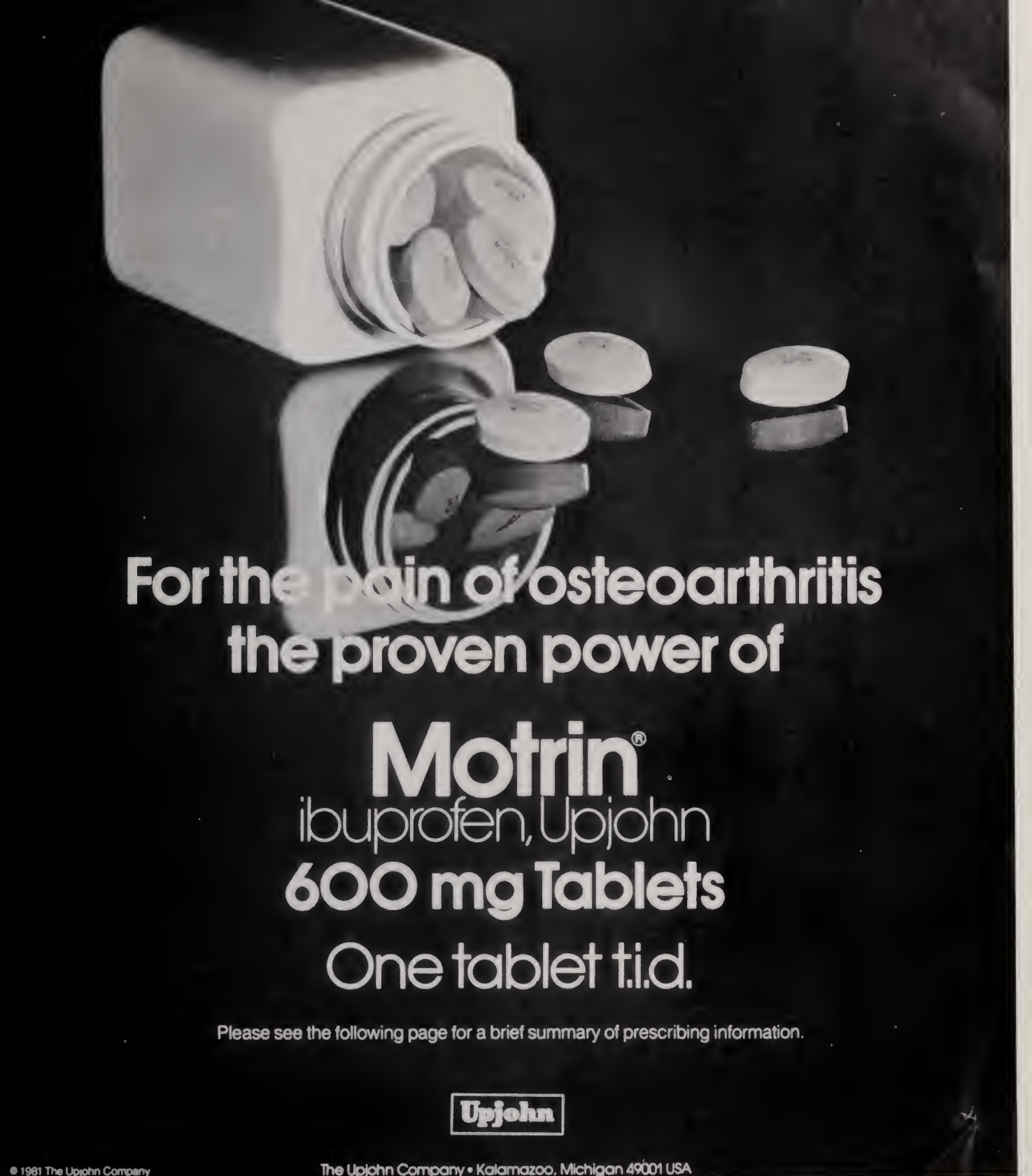

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Motrin® Tablets (ibuprofen, Upjohn)

Contraindications: Individuals hypersensitive to it or with the syndrome of nasal polyps, angioedema, and bronchospastic reactivity to aspirin, iodides or other non-steroidal anti-inflammatory agents. Anaphylactoid reactions have occurred in such patients.

Warnings: Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation and bleeding may end fatally. An association has not been established. *Motrin* should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If *Motrin* must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

Chronic studies in rats and monkeys have shown mild renal toxicity characterized by papillary edema and necrosis. Renal papillary necrosis has rarely been shown in humans treated with *Motrin*.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue *Motrin* and the patient should have an ophthalmologic examination, including central visual fields and color vision testing. **Fluid retention and edema** have been associated with *Motrin*; use with caution in patients with a history of cardiac decompensation or hypertension. *Motrin* is excreted mainly by the kidneys. In patients with renal impairment, reduced dosage may be necessary. Prospective studies of *Motrin* safety in patients with chronic renal failure have not been done. *Motrin* can inhibit **platelet aggregation** and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy. Patients should report signs or symptoms of **gastrointestinal ulceration** or bleeding, blurred vision or other eye symptoms, skin rash, weight gain or edema. To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when *Motrin* is added. The anti-pyretic, anti-inflammatory activity of *Motrin* may mask inflammation and fever.

Drug interactions: *Aspirin* used concomitantly may decrease *Motrin* blood levels. Coumarin bleeding has been reported in patients taking *Motrin* and coumarin.

Pregnancy and nursing mothers. *Motrin* should not be taken during pregnancy nor by nursing mothers.

Adverse Reactions

The most frequent type of adverse reaction occurring with *Motrin* is gastrointestinal, of which one or more occurred in 4% to 16% of the patients.

Incidence Greater Than 1% (but less than 3%)—Probable Causal Relationship

Gastrointestinal: Nausea*, epigastric pain*, heartburn*, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of GI tract (bloating and flatulence). **Central Nervous System:** Dizziness*, headache, nervousness. **Dermatologic:** Rash* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic/Endocrine:** Decreased appetite. **Cardiovascular:** Edema, fluid retention (generally responds promptly to drug discontinuation; see PRECAUTIONS).

*Incidence Less Than 1%—Probable Causal Relationship***

Gastrointestinal: Gastric or duodenal ulcer with bleeding and/or perforation, gastrointestinal hemorrhage, melena, gastritis, hepatitis, jaundice, abnormal liver function tests. **Central Nervous System:** Depression, insomnia, confusion, emotional lability, somnolence, aseptic meningitis with fever and coma. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme, Stevens-Johnson syndrome, alopecia. **Special Senses:** Hearing loss, amblyopia (blurred and/or diminished vision, scotomata and/or changes in color vision); see PRECAUTIONS). **Hematologic:** Neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia (sometimes Coombs' positive), thrombocytopenia with or without purpura, eosinophilia, decreases in hemoglobin and hematocrit. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure, palpitations. **Allergic:** Syndrome of abdominal pain, fever, chills, nausea and vomiting, anaphylaxis, bronchospasm (see CONTRAINDICATIONS). **Renal:** Acute renal failure in patients with preexisting significantly impaired renal function, decreased creatinine clearance, polyuria, azotemia, cystitis, hematuria. **Miscellaneous:** Dry eyes and mouth, gingival ulcerations.

*Incidence Less Than 1%—Causal Relationship Unknown***

Gastrointestinal: Pancreatitis. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities, pseudotumor cerebri. **Dermatologic:** Toxic epidermal necrolysis, photoallergic skin reactions. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Bleeding episodes (e.g., epistaxis, menorrhagia). **Metabolic/Endocrine:** Gynecomastia, hypoglycemic reaction. **Cardiovascular:** Arrhythmia (sinus tachycardia, sinus bradycardia). **Allergic:** Serum sickness, lupus erythematosus syndrome, Henoch-Schonlein vasculitis. **Renal:** Renal papillary necrosis.

*Reactions occurring in 3% to 9% of patients treated with *Motrin*. (Those reactions occurring in less than 3% of the patients are unmarked.)

**Reactions are classified under *"Probable Causal Relationship" (PCR)* if there has been one positive rechallenge or if three or more cases occur which might be causally related. Reactions are classified under *"Causal Relationship Unknown"* if seven or more events have been reported but the criteria for PCR have not been met.

Overdosage: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine, so alkaline diuresis may be beneficial.

Dosage and Administration: Do not exceed 2400 mg per day. If gastrointestinal complaints occur, administer with meals or milk.

Rheumatoid arthritis and osteoarthritis, including flares of chronic disease. Suggested dosage is 300, 400, or 600 mg t.i.d. or q.i.d. Mild to moderate pain, 400 mg every 4 to 6 hours as necessary for relief of pain.

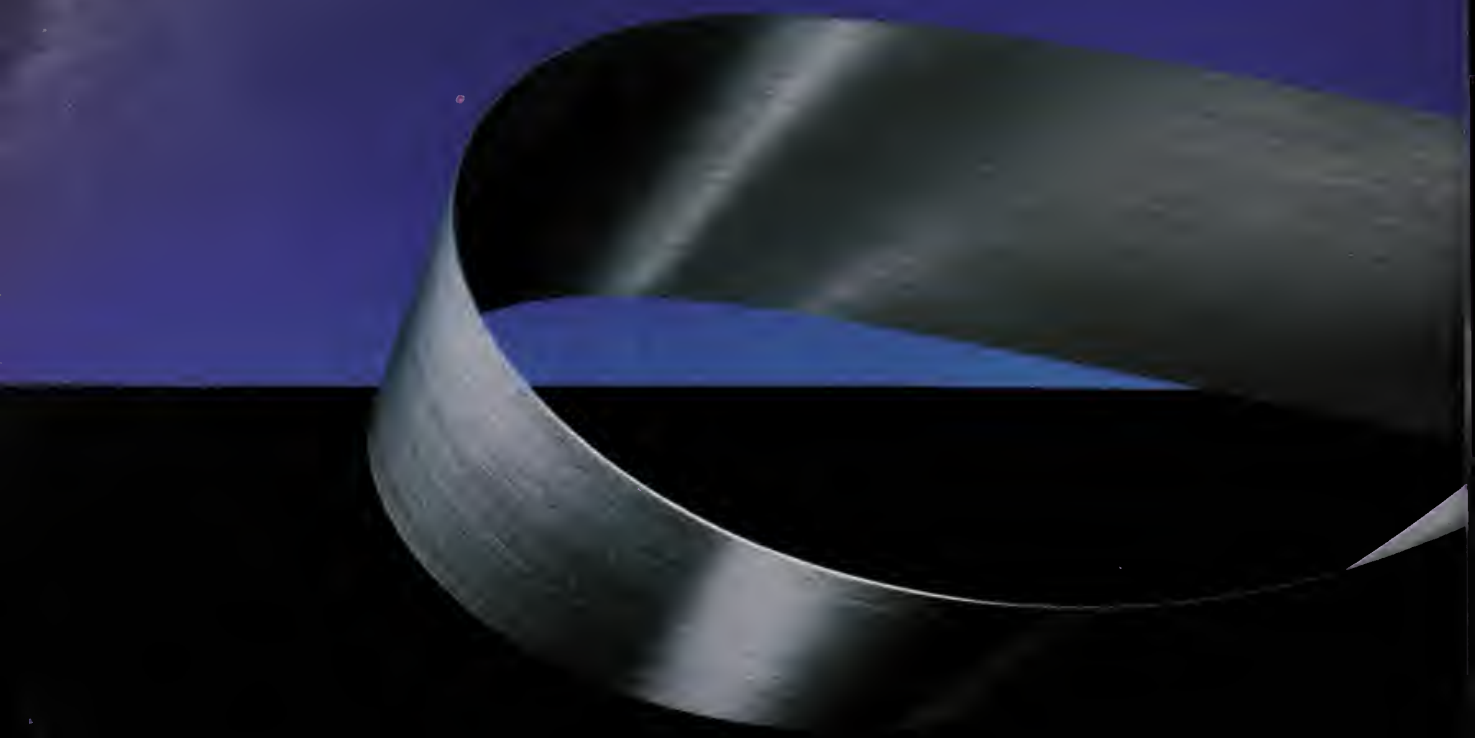
Caution: Federal law prohibits dispensing without prescription.

Upjohn THE UPJOHN COMPANY
Kalamazoo, Michigan 49001 USA

J-9042-4 MED B-5-S July 1981

NEW...from Boehringer Ingelheim Ltd.

Respbid™...the theophyllin
(theophylline)



The Möbius Strip—a revolution in surface geometry

The Möbius Strip, discovered by August Möbius (1790-1868), is a unique geometrical figure. It is a two-dimensional object existing in three-dimensional space, having one plane surface and one edge, and forming a continuum which has intrigued generations of mathematicians and non-mathematicians alike.

If you'd like an authentic Möbius Strip plus a description of its mathematical and historical significance, please see your Boehringer Ingelheim Ltd. representative, or write Boehringer Ingelheim Ltd. directly.

Sustained release Respbid™ keeps working hour after hour

Respbid helps keep blood levels within the drug's therapeutic range 24 hours per day on a b.i.d. dosage

Effective for up to 12 hours*

Easy to build dose control

- twice daily dosage
- two strengths: 250 mg and 500 mg tablets
- scored tablets to aid dose titration

The Respbid sustained release formulation taken every 12 hours provides a theophylline continuum... the benefit, easier breathing round-the-clock with relatively stable serum levels

*Dosage needed to achieve a therapeutic theophylline blood level depends upon the rate of elimination. which may vary from patient to patient

Please see following page for brief summary of prescribing information, including warnings. precautions, and adverse reactions.

Respbid™
(theophylline) Sustained Release Tablets of 250 mg and 500 mg
Bronchodilator

NEW...from Boehringer Ingelheim Ltd.

Respbid™...the theophylline continuum
(theophylline)

Relatively stable theophylline serum levels to provide easier breathing round-the-clock

Respbid™
(theophylline) Sustained Release Tablets of 250 mg and 500 mg
Bronchodilator

Respbid™ (theophylline)
Oral Bronchodilator

Sustained Release
Tablets of 250 mg and 500 mg

Indications: For relief of acute bronchial asthma and for reversible bronchospasm associated with chronic bronchitis and emphysema

Contraindications: In individuals who have shown hypersensitivity to any of its components

Warnings: Status asthmaticus is a medical emergency. Optimal therapy frequently requires additional medication including corticosteroids when the patient is not rapidly responsive to bronchodilators.

Excessive theophylline doses may be associated with toxicity and serum theophylline levels are recommended to assure maximal benefit without excessive risk. Incidence of toxicity increases at levels greater than 20 mcg/ml. Morphine, curare, and stilbamidine should be used with caution in patients with airflow obstruction since they stimulate histamine release and can induce asthmatic attacks. They may also suppress respiration leading to respiratory failure. Alternative drugs should be chosen whenever possible.

There is an excellent correlation between high blood levels of theophylline resulting from conventional doses and associated clinical manifestations of toxicity in (1) patients with lowered body plasma clearances (due to transient cardiac decompensation), (2) patients with liver dysfunction or chronic obstructive lung disease, (3) patients who are older than 55 years of age, particularly males.

There are often no early signs of less serious theophylline toxicity such as nausea and restlessness, which may appear in up to 50 percent of patients prior to onset of convulsions. Ventricular arrhythmias or seizures may be the first signs of toxicity.

Many patients who have higher theophylline serum levels exhibit a tachycardia.

Theophylline products may worsen pre-existing arrhythmias.

Usage in Pregnancy: Safe use in pregnancy has not been established relative to possible adverse effects on fetal development, but neither have adverse effects on fetal development been established. This is unfortunately true for most antiasthmatic medications. Therefore, use of theophylline in pregnant women should be balanced against the risk of uncontrolled asthma.

Precautions: Mean half-life in smokers is shorter than non-smokers, therefore smokers may require larger doses of theophylline. Theophylline should not be administered concurrently with other xanthine medications. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, liver disease, and in the elderly (especially males) and in neonates. Great caution should especially be used in giving theophylline to patients in congestive heart failure. Such patients have shown markedly prolonged theophylline blood level curves with theophylline persisting in serum for long periods following discontinuation of the drug.

Use theophylline cautiously in patients with history of peptic ulcer.

Theophylline may occasionally act as a local irritant to G.I. tract although gastrointestinal symptoms are more commonly central and associated with serum concentrations over 20 mcg/ml.

Adverse Reactions: The most consistent adverse reactions are usually due to overdose and are:
1. Gastrointestinal: nausea, vomiting, epigastric pain, hematemesis, diarrhea
2. Central nervous system: headache, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.
3. Cardiovascular: palpitation, tachycardia, extra systoles, flushing, hypotension, circulatory failure, life-threatening ventricular arrhythmias.
4. Respiratory: tachypnea
5. Renal: albuminuria, increased excretion of renal tubular potentiation or diuresis, and red blood cells
6. Others: hyperglycemia and inappropriate ADH syndrome

Drug Interactions: Toxic synergism with ephedrine has been documented and may occur with some other sympathomimetic bronchodilators.

Drug	Effect
Aminophylline with Lithium Carbonate	Increased excretion of Lithium Carbonate
Aminophylline with Propranolol	Antagonism of Propranolol effect
Theophylline with Furosemide	Increased diuresis of Furosemide
Theophylline with Hexamethonium	Decreased Hexamethonium-induced chromatropic effect
Theophylline with Reserpine	Reserpine-induced tachycardia
Theophylline with Chlordiazepoxide	Chlordiazepoxide-induced fatty acid mobilization
Theophylline with Cyclamycin (TAO=Triacetyloleandomycin), erythromycin, lincomycin	Increased Theophylline plasma levels

Caution: Federal law prohibits dispensing without prescription.

For complete details, please see full prescribing information.

Boehringer Ingelheim

Boehringer Ingelheim Ltd
Ridgefield, CT 06877

Bactrim™
(trimethoprim and sulfamethoxazole)
succeeds

Bactrim is useful for the following infections when due to susceptible strains of indicated organisms (see indications section in summary of product information):

Expanding its usefulness in antimicrobial therapy

in recurrent UTI...
a continuing record of high clinical effectiveness against common uropathogens

in acute otitis media in children...
effective against both major otic pathogens...with *b.i.d.* convenience

in acute exacerbations of chronic bronchitis in adults...
clears the sputum and lowers its volume...on *b.i.d.* dosage

in shigellosis...
faster relief of diarrhea than with ampicillin[2]

Before prescribing, please consult complete product information, a summery of which follows:

Indications and Usage: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris, Proteus morganii.* It is recommended that initial episodes of uncompilcated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. *Note:* The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

For acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over other antimicrobials. Limited clinical information presently available on effectiveness of treatment of otitis media with Bactrim when infection is due to ampicillin-resistant *Haemophilus influenzae*. To date, there are limited data on the safety of repeated use of Bactrim in children under two years of age. Bactrim is not indicated for prophylactic or prolonged administration in otitis media at any age.

For acute exacerbations of chronic bronchitis in adults due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over a single antimicrobial agent.

For enteritis due to susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

Also for the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; patients with documented megaloblastic anemia due to folate deficiency; pregnancy at term; nursing mothers because sulfonamides are excreted in human milk and may cause kernicterus; infants less than 2 months of age

Warnings: BACTRIM SHOULD NOT BE USED TO TREAT STREPTOCOCCAL PHARYNGITIS. Clinical studies show that patients with group A β-hemolytic streptococcal tonsillopharyngitis have higher incidence of bacteriologic failure when treated with Bactrim than do those treated with penicillin. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

Precautions: *General:* Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function. Bactrim may prolong prothrombin time in those receiving warfarin; reassess coagulation time when administering Bactrim to these patients.

Pregnancy: Teratogenic Effects: Pregnancy Category C. Because trimethoprim and sulfamethoxazole may interfere with folic acid metabolism, use during pregnancy only if potential benefits justify the potential risk to the fetus.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for infants less than two months of age.

URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN, AND ACUTE OTITIS MEDIA IN CHILDREN:

Adults: Usual adult dosage for urinary tract infections—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days. Use identical daily dosage for 5 days for shigellosis.

Children: Recommended dosage for children with urinary tract infections or acute otitis media—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. Use identical daily dosage for 5 days for shigellosis.

For patients with renal impairment: Use recommended dosage regimen when creatinine clearance is above 30 ml/min. If creatinine clearance is between 15 and 30 ml/min, use one-half the usual regimen. Bactrim is not recommended if creatinine clearance is below 15 ml/min.

ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS IN ADULTS:

Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 14 days.

PNEUMOCYSTIS CARINII PNEUMONITIS:

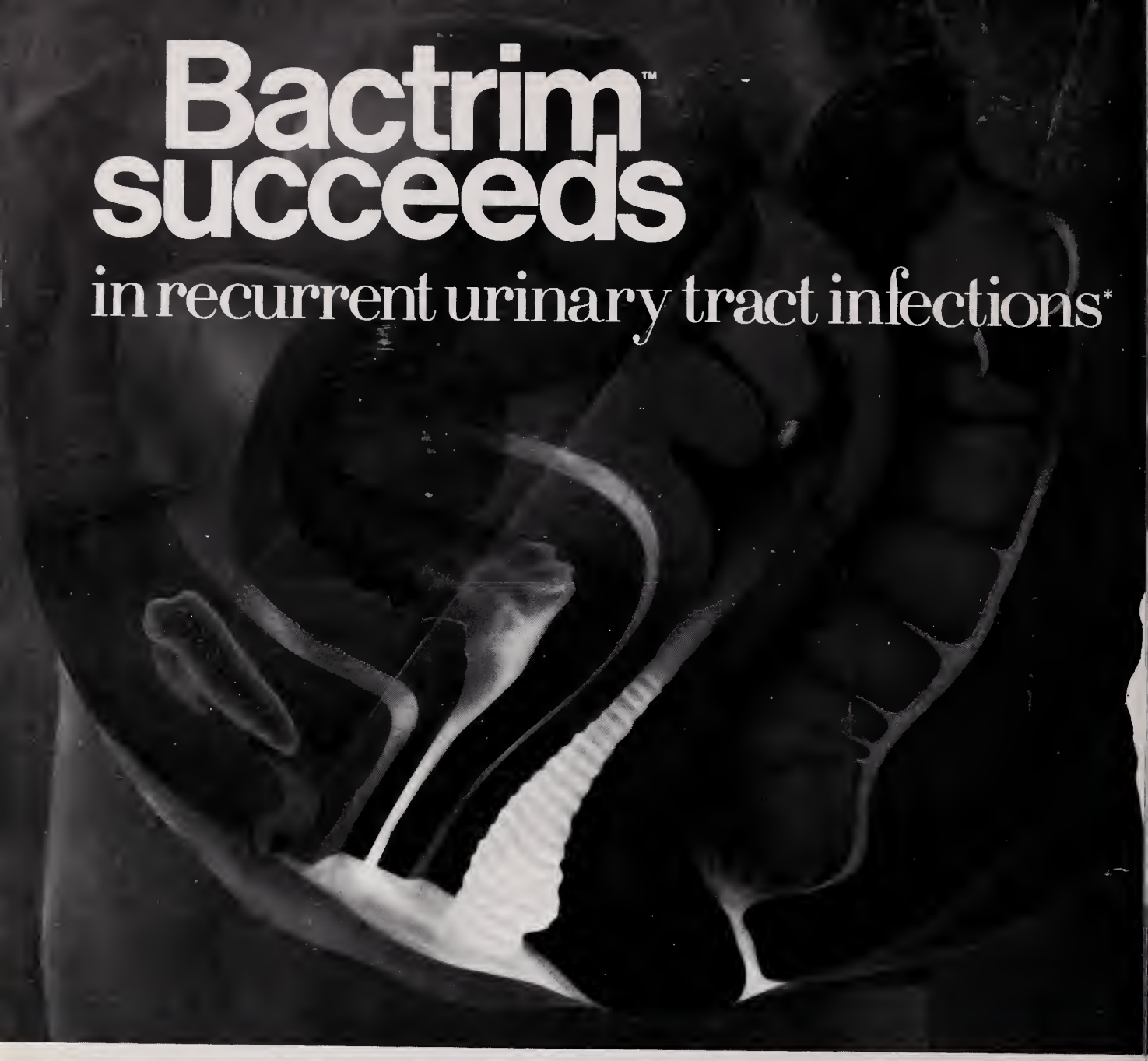
Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

Supplied: *Double Strength (DS) tablets*, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100; Prescription Paks of 20 and 28. *Tablets*, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40. *Pediatric Suspension*, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); cherry-flavored—bottles of 100 ml and 16 oz (1 pint). *Suspension*, containing 40 mg trimethoprim and 200 mg sulfamethoxazole per teaspoonful (5 ml); fruit-licorice flavored—bottles of 16 oz (1 pint).

ROCHE®
ROCHE LABORATORIES
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

Bactrim™ succeeds

in recurrent urinary tract infections*



from site to source

Bactrim continues to demonstrate high clinical effectiveness in recurrent urinary tract infections. Bactrim reaches effective levels in urine, serum, and renal tissue[1]...the trimethoprim component diffuses into vaginal secretions in bactericidal concentrations[1]... and in the fecal flora, Bactrim effectively suppresses Enterobacteriaceae[1,2] with little resulting emergence of resistant organisms.

1. Rubin RH, Swartz MN: *N Engl J Med* 303:426-432, Aug 21, 1980. 2. Data on file, Medical Department, Hoffmann-La Roche Inc.

Bactrim™ DS

160 mg trimethoprim and 800 mg sulfamethoxazole

DOUBLE STRENGTH TABLETS

maximizes results with B.I.D. convenience

ROCHE®

*due to susceptible strains of indicated organisms

Please see previous page for summary of product information.

ASOCIACION MEDICA DE PUERTO RICO

BOLETIN

VOL. 74/NUM. 2 FEBRERO 1982

For IPPB therapy and hand nebulizer

Alupent® Inhalant Solution

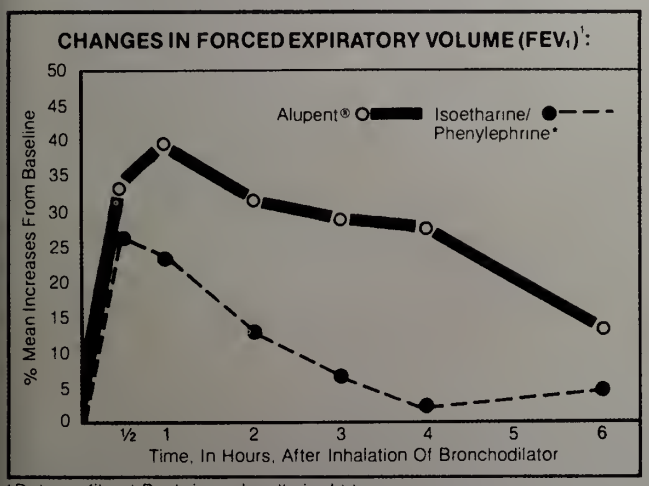
(metaproterenol sulfate) 5%

long needed...long lasting

A bronchodilator for relief of reversible bronchospasm associated with bronchitis, emphysema, and bronchial asthma.

- The Solution with a long duration of action

Up to 6 hours when administered by IPPB



1 Data on file at Boehringer Ingelheim Ltd.

*This combination is no longer being manufactured in the United States. Isoetharine is now available as a single entity 1.0% solution.

- Prompt onset
- Effective for long-term use
- Adverse reactions similar to those of other sympathomimetic agents

How to use Alupent® Inhalant Solution (metaproterenol sulfate)

Method of Administration	Usual Single Dose	Frequency of Use	Range	Dilution
IPPB	0.3 ml	•For acute attacks—every 4 hrs. •For chronic bronchospastic pulmonary diseases-3 to 4 times a day.	0.2-0.3 ml	Diluted in approximately 2.5 ml of saline solution or other diluent
Hand Nebulizer	10 Inhalations	•For acute attacks—every 4 hrs. •For chronic bronchospastic pulmonary diseases-3 to 4 times a day.	5-15 inhalations	No Dilution

Please see brief summary on last page of this ad, for warnings, precautions and adverse reactions.

Alupent®

(metaproterenol sulfate)

Inhalant Solution

Bronchodilator

Alupent®
(metaproterenol sulfate)
Inhalant Solution
Bronchodilator

Alupent® (metaproterenol sulfate)
Inhalant Solution

Contraindications: Use in patients with cardiac arrhythmias associated with tachycardia is contraindicated.

Warnings: Excessive use of adrenergic aerosols is potentially dangerous. Fatalities have been reported following excessive use of Alupent, brand of metaproterenol sulfate, as with other sympathomimetic inhalation preparations, and the exact cause is unknown. Cardiac arrest was noted in several cases. Paradoxical bronchoconstriction with repeated excessive administration has been reported with sympathomimetic agents. Patients should be advised to contact their physician in the event that they do not respond to their usual dose of a sympathomimetic amine aerosol.

Precautions: Because Alupent, brand of metaproterenol sulfate, Inhalant Solution is a sympathomimetic drug, it should be used with great caution in patients with hypertension, coronary artery disease, congestive heart failure, hyperthyroidism or diabetes, or when there is sensitivity to sympathomimetic amines.

Information for Patients: Extreme care must be exercised with respect to the administration of additional sympathomimetic agents. A sufficient interval of time should elapse prior to administration of another sympathomimetic agent.

Carcinogenesis. Long-term studies in mice and rats to evaluate the oral carcinogenic potential of metaproterenol sulfate have not been completed.

Pregnancy: Teratogenic Effects: Pregnancy Category C. Alupent, brand of metaproterenol sulfate, has been shown to be teratogenic and embryocidal in rabbits when given orally in doses 620 times the human inhalation dose; the teratogenic effects included skeletal abnormalities and hydrocephalus with bone separation. Oral reproduction studies in mice, rats and rabbits showed no teratogenic or embryocidal effect at 50 mg/kg, or 310 times the human inhalation dose. There are no adequate and well-controlled studies in pregnant women. Alupent, brand of metaproterenol sulfate, Inhalant Solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Alupent, brand of metaproterenol sulfate, is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of Alupent Inhalant Solution in children below the age of 12 have not been established.

Adverse Reactions: Adverse reactions are similar to those noted with other sympathomimetic agents.

The most frequent adverse reactions to Alupent, brand of metaproterenol sulfate, are nervousness, tachycardia, tremor and nausea. Less frequent adverse reactions are hypertension, palpitations, vomiting and bad taste.

Overdosage: The symptoms of overdosage are those of excessive beta adrenergic stimulation listed under **Adverse Reactions.** These reactions usually do not require treatment other than reduction of dosage and/or frequency of administration.

How Supplied: Alupent, brand of metaproterenol sulfate, Inhalant Solution is supplied as a 5% solution in bottles of 10 ml with accompanying calibrated dropper. Store at room temperature; avoid excessive heat. Protect from light.

For complete details, please see full prescribing information.

Distributed by:
Boehringer Ingelheim Ltd.
Ridgefield, CT 06877

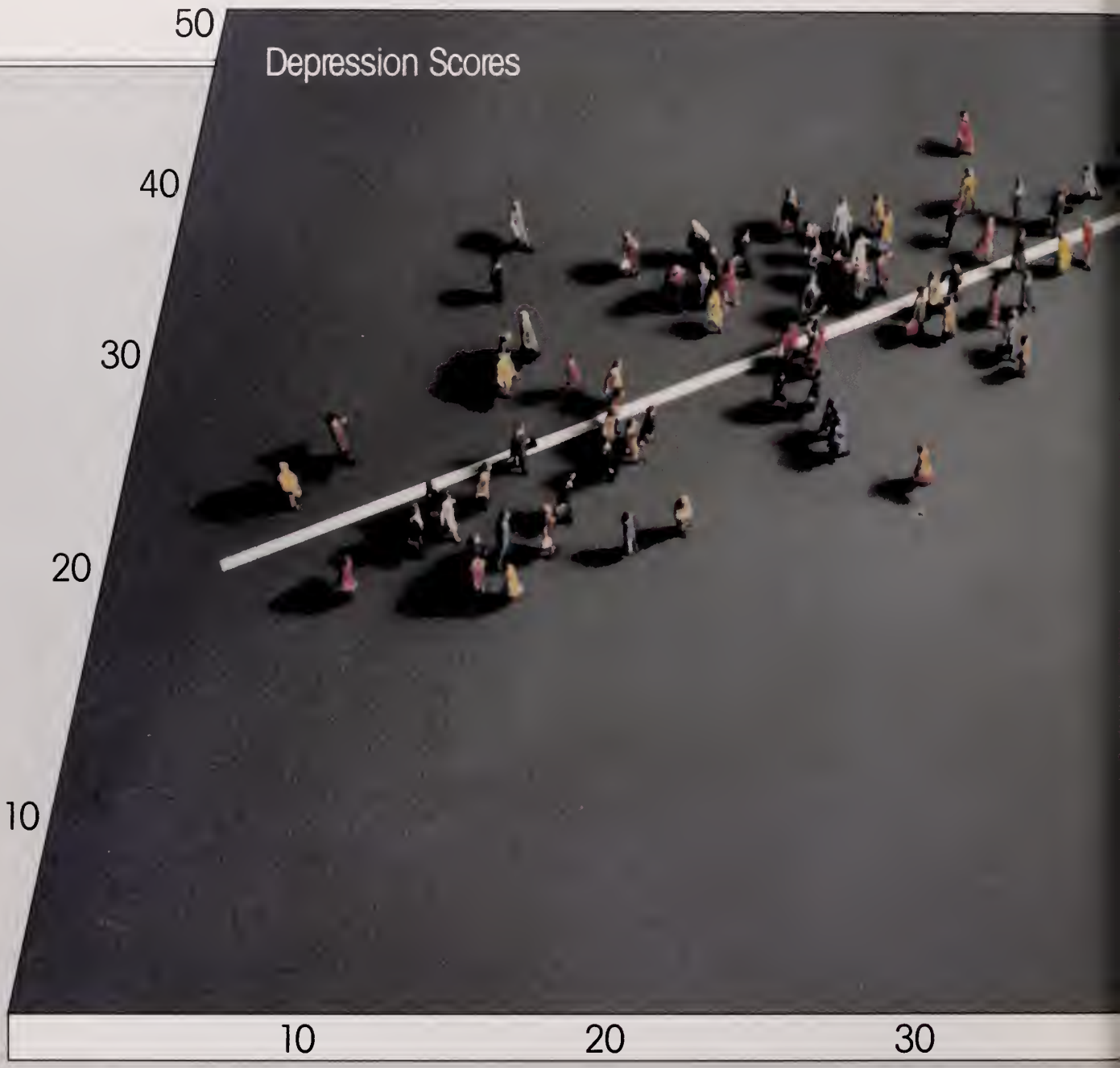
Under license from Boehringer Ingelheim GmbH

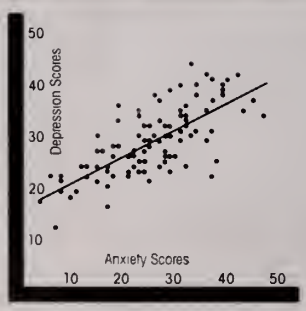
ASOCIACION MEDICA DE PUERTO RICO

BOLETiN

VOL. 74 - NUM. 2
FEBRERO 1982
ORGANO OFICIAL

FOR THE 7 OF 10 NONPSYCHOTIC





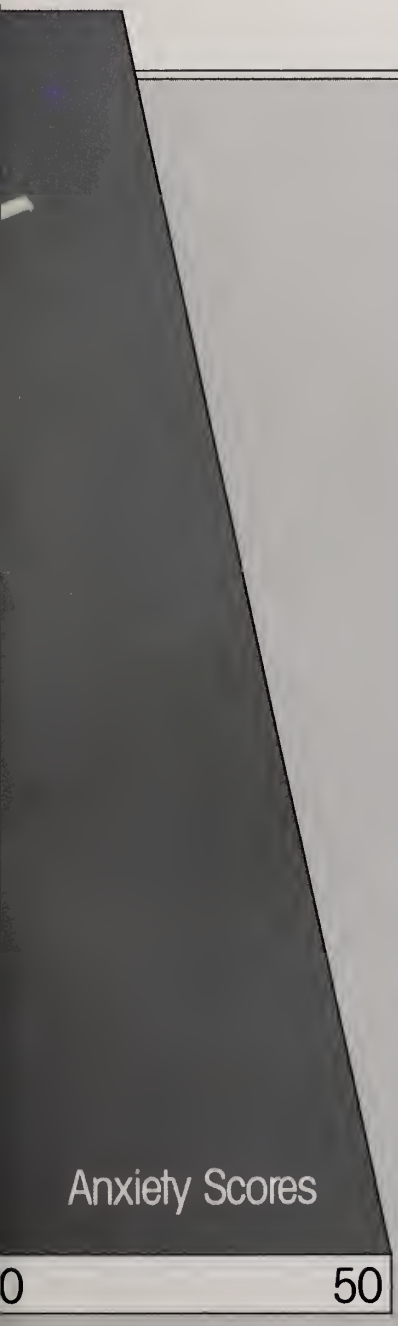
Clear correlation between anxiety and depression[3]

The above graph illustrates a relationship between anxiety and depression, indicating that patients seldom present with anxiety or depression alone; more often they have both in varying degrees. Data based on a sampling of 100 outpatients (64 male; 36 female) seen at a general psychiatric clinic.

[3]Adapted from Cloghorn, J. The anxiety-depression syndrome. *Psychosomatics 11*:438-441, Sept-Oct 1970.

ROCHE

DEPRESSED PATIENTS WHO ARE ALSO ANXIOUS[1,2]



Most depressed patients are also anxious...

Some authors estimate that 70% of all nonpsychotic patients with symptoms of depression have concomitant symptoms of anxiety.[1,2] One author found a distinct correlation between anxiety and depression scores in 100 nonpsychotic outpatients administered the Minnesota Multiphasic Personality Inventory in a general psychiatric clinic.[3] As depression scores increased, so did anxiety scores. No attempt was made to select patients other than to exclude psychotics.

but not psychotic

The logic of treating both components of anxious depression is clear. Antipsychotics, like the phenothiazines, however, carry a well-documented risk of tardive dyskinesia.[4] Because of this, an APA Task Force recently recommended the judicious use of phenothiazines in cases other than chronic psychosis or the use of alternative treatments.

A better way to give relief

Limbitrol combines the specific anxiolytic action of Librium® (chlordiazepoxide HCl/Roche)—a benzodiazepine with a long history of safe use—with the antidepressant action of amitriptyline, a tricyclic of established clinical efficacy. In comparison to phenothiazines, Limbitrol and its components have rarely been associated with tardive dyskinesia or other extrapyramidal side effects. And in terms of rapid response and patient compliance, Limbitrol appears to be superior to amitriptyline alone. Controlled multiclinic studies showed Limbitrol relieved more symptoms more rapidly than did amitriptyline.[5] Despite a higher incidence of drowsiness, the dropout rate due to side effects was lower with Limbitrol. (See adverse reactions section in summary of product information on next page. As with any CNS-acting agent, patients should be cautioned about driving or using dangerous machines while on therapy with Limbitrol.)

References: 1. Rickels K: Drug treatment of anxiety, in *Psychopharmacology in the Practice of Medicine,* ed. Jarvik ME. New York, Appleton-Century-Crofts, 1977, p. 316. **2.** Schatzberg AF, Cole JO: Benzodiozepines in depressive disorders. *Arch Gen Psychiatry 35:*1359-1365, 1978. **3.** Cloghorn J: The anxiety-depression syndrome. *Psychosomatics 11:*438-441, 1970. **4.** The Task Force on Late Neuralagicol Effects of Antipsychotic Drugs: Tordive dyskinesio, summary of o task force report of the American Psychiatric Association. *Am J Psychiatry 137:*1163-1172, 1980. **5.** Feighner JP *et ol:* A placebo-controlled multicenter triol of Limbitrol versus its components (amitriptyline ond chlordiozepoxide) in the symptomatic treatment of depressive illness. *Psychophormacology 61:*217-225, 1979.

In moderate depression and anxiety

Limbitrol® IV

Tablets 5-12.5 each contoining 5 mg chlordiazepoxide ond 12.5 mg omitriptyline (os the hydrochloride salt)

Tablets 10-25 each containing 10 mg chlordiozepoxide ond 25 mg omitriptyline (os the hydrochloride salt)

Relief without a phenothiazine

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NUESTRA PORTADA

Obra en acuarela titulada "Garita" de la artista Margarita García Díaz.

La autora nació en Santurce, Puerto Rico y se inició en la pintura en el Colegio de la Inmaculada. Allí estudió óleo y dijubo al carbón bajo la dirección de Sor Alicia Calderón. Mas tarde realizó estudios universitarios en el Departamento de Bellas Artes de la Universidad de Puerto Rico donde se graduó con honores.

Actualmente trabaja perfeccionando la técnica de la acuarela bajo la dirección de la profesora Myriam de Sureda.

Margarita es esposa del Dr. Luis Ruiz Rivera, ex-secretario de la Sección de Pediatría de la Asociación Médica de Puerto Rico.

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COLUMNA DEL EDITOR

Es con gran satisfacción que me dirigo a la matrícula de nuestra Asociación y a los lectores del Boletín de la Asociación Médica de Puerto Rico desde esta primera "Columna del Editor". La razón de ser de la misma es mantener informados a nuestros lectores sobre el estado de nuestra publicación, las actualidades que le atañen, y las constantes proyecciones futuras.

Debo comenzar señalando la favorable acogida que ha tenido el nuevo formato del Boletín. Este éxito fue en gran parte debido al apoyo y cooperación prestados por nuestro Director Ejecutivo, el Sr. Diego Román, y el Sr. José Villavicencio, publicista y diseñador gráfico. En lo sucesivo ellos tendrán a su cargo las funciones administrativas del Boletín, incluyendo su promoción, difusión, y mejoramiento artístico, gestiones de gran importancia para que nuestro órgano oficial sea de la más alta calidad. Esta publicación tiene que reflejar la imagen de prestigio que merece la profesión médica de nuestro país.

Vaya mi reconocimiento a la casa impresora Art Printing y su personal por el esfuerzo realizado y "horas extra" compartidas para lograr la publicación del primer número en el tiempo previsto.

En este número contamos con una nueva sección: *Legislaciones de Salud,* la cual les invito a leer. La misma consiste de abstractos de todos los proyectos presentados en nuestras Cámaras Legislativas que tienen relación directa o indirecta con la salud del pueblo y el ejercicio de nuestra profesión. Nos consta que la mayoría de estas piezas legislativas no aparecen en la prensa, aún después de convertirse en ley, y creemos que es función del Boletín el informar a sus lectores sobre este aspecto también importante en el rol del médico en nuestra sociedad.

Por último, paso a comentar sobre nuestra portada, que como habrán leído es obra de la esposa de uno de nuestros miembros lo cual es de gran significado. Este hecho refleja participación a todos los niveles, que constituye uno de nuestros objetivos principales. Queremos que la mayor parte del Boletín sea producto de nuestros miembros y sus relacionados, pues de ellos es la revista y a ellos nos debemos en la misión que nos fue encomendada. Por esa razón nuestro esfuerzo tiene que ser constante y de carácter progresivo para poder lograr lo que los miembros de la Asociación Médica de Puerto Rico se merecen: lo mejor.

Rafael Villavicencio, MD
Presidente
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EDITORIAL

La Tomografía Computarizada: Ha Llegado A Su Madurez Científica

La tomografía computarizada ha llegado a su madurez científica, y ha dejado de ser, como se vaticinó en un tiempo, una curiosidad médica.

El premio Nobel en medicina fue concedido a los inventores del método, y después de diez años de uso clínico, el entusiasmo generado inicialmente es ahora aun mayor.

El viejo Zorro de la cirugía puertorriqueña, Dr. Frank Raffuci, decía que la indicación para una traqueotomía era que usted pensara sobre hacerla. Yo me siento de la misma manera hacia la tomografía computarizada de cerebro. El método es no invasivo, con una exactitud de diagnóstico superior a la combinación de otras modalidades, y sin la necesidad de hospitalización o cuidado post estudio. La única contraindicación parcial sería la presencia de reacciones alérgicas previas a inyecciones de medios de contraste, y solamente parcial, porque la inyección de contraste se puede obviar, particularmente con equipo de última generación, sin afectar la exactitud del diagnóstico. Siendo así, el estudio se ha convertido en el arma primaria diagnósitca en pacientes en que se sospecha una lesión intracraneal. El poder contar con este recurso sin duda ha resultado en una verdadera revolución para las especialidades neurológicas, pues facilita el diagnóstico temprano aún en pacientes difíciles de manejar, tales como niños, traumatizados, ancianos y otros pacientes similares.

Al principio hubo cierta reserva a una utilización más frecuente por miedo a la radiación generada, pero con las máquinas de primera y segunda generación, la cantidad de radiación recibida no era mayor que la que un paciente recibía al hacérsele placas de craneo, angiografía, pneumoencefalografía y estudios de medicina nuclear. Con el equipo moderno esa radiación se reduce lo suficiente como para no ser un factor a considerar cuando se piensa ordenar un estudio.

Como dije antes, la exactitud del método es excelente, y la incidencia de falsos positivos ha ido disminuyendo de un 11-12% en las series iniciales a menos de un 5% en las reportadas recientemente.

No es raro, entonces, que de ser mi método complementario de diagnóstico, haya evolucionado a ser el método de preferencia en lesiones cerebrales, superior por su sencillez y rendimiento a todos los otros métodos existentes. En mi opinión, que admito es prejuiciada, la tomografía computarizada de cerebro representa el mayor avance en métodos de diagnóstico por imagen desde el descubrimiento de Rayos X, y su impacto ha sido instrumental en producir un diagnóstico más rapidamente.

El método ha llegado a un punto de desarrollo donde los avances de ahora en adelante serán pocos y lentos, pero lo que tenemos es suficiente para beneficiar grandemente un número de pacientes que hace algunos años hubieran necesitado una batería de pruebas para obtener los mismos resultados.

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CT Scan Diagnosis of Parenchymatous Cerebral Metastases

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Summary: **Factors that in conjunction favor metastases over primary brain tumor by CT scanning:**

1. **More than one lesion.**
2. **Situation at the junction between the gray and white matter.**
3. **Homogeneous nodular mass or ring aspect.**
4. **(a) Disproportionately large amount of vasogenic edema.**
   (b) A significant decrease in size of the edematous region within the first 24 hours after steroid therapy in serial CT scans.
5. **Localization in an adult of tumor in the posterior fossa.**
6. **Evidence of intracranial hemorrhage.**

Factors against the diagnosis of metastases:

1. **Edema other than vasogenic.**
2. **Presence of calcifications.**
3. **A tumor size of more than 100 mm. along its longest axis.**

CT scanning has proven to be a revolutionary tool in the diagnosis of brain tumors. It allows one to distinguish a neoplasm from subdural or intracerebral hematomas, infarcts or abscess, which under some circumstances may mimic the clinical course of a tumor[1]. Yet, it has been stated that in case of a single lesion, a CT scan alone cannot differentiate between a glioma and metastases[2]. It is the purpose of this article to stress certain CT scan particularities whereby such a distinction can be made.

Among the multiplicity of intracranial diseases, tumor is exceeded in frequency only by stroke[3]. Of those patients who die of cancer, necropsy series vary widely in regards to the incidence of metastases involving the brain and its coverings; being as low as 4.2 percent in some, to as high as 37 percent in others[4]. It is suspected that this frequency is presently rising due to the use of chemotherapeutic agents that do not cross the blood-brain barrier providing systemic control and extending survival but permitting CNS metastases to become manifest[5 6].

Parenchymal involvement is most common with carcinoma of the lung (38 percent), breast (24 percent) and melanomas (8 percent). Other sites are less frequent; both those from the gastrointestinal tract (especially colon and rectum) and the genitourinary tract (hypernephroma, uterine carcinoma and prostate carcinoma) accounting for only 11 percent. There remains about 14 percent of cases from an unknown primary site[7].

All areas of the brain may be affected, but not to the same extent. Most occur in the distribution of the middle cerebral artery, with 55 percent posterior to the Rolandic fissure[8]. Metastases preferentially involve the junction between the gray and white matter presumably because tumor cells embolize through the arterial system and there is a rapid arteriolar narrowing at the site. Another explanation invokes the dense capillary plexus in that area, with consequent slowing of blood flow and a better chance for the tumorous emboli to implant itself[9]. Localization in an adult of a neoplasia in the posterior fossa would also suggest a secondary brain tumor. Autopsy studies reveal that 30 percent of metastatic tumors are infratentorial[10]. Primary brain tumors although commonly found in the posterior fossa during childhood become less aparent wich increasing age. Glioblastoma multiforme per se, is rarely found during adulthood in this location[11].

Multiple lesions are suggestive of metastases. Previous studies[12] stated that multifocality was the rule for secondary brain tumors, while only 2.5 to 4.9 percent of all primary gliomas are multicentric[4]. Present series have changed their proportions; 59.9 percent of metastases being reported as single lesions[13]. There is also a high incidence (31 percent) of those discovered before the primary tumor has been detected[13]. Better diagnostic methods, such as CT scan may have played a role in this regard.

Mean survival after diagnosis depends on whether the lesion is single or multiple and whether the patient receives some form of treatment; prognosis is either way dismal ranging in the average from 7.5 to 15 weeks[13]. Not uncommonly however, some patients last several years. The most important factor accounting for the dim outcome of patients with cerebral metastases is brain edema and consequent herniation. Edema is of the vasogenic type, the same kind seen with abscess, hemorrhage, contusion and even lead encephalopathy[14]. It is generally attributed to a disturbance of vascular permeability; possibly the rapid expansive-mass growth* effect of some of these lesions, partly collapse the capacitance venous vessels with retorgrade increase in intraluminal pressure and escape of water and plasma constituents from the capillaries to the parenchyma. Fenestration of blood vessels within the metastases[15 16], may also offer a partial explanation in some

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* *Contrariwise, gliomas grow primarily by infiltration.*

cases. Vasogenic edema affects primarily, for reasons not well understood, the white matter[12]. It is observed by CT scan as a diffuse area of decrease attenuation values interdigitating with the "apparently" unaffected cortex (Fig. 1). Serial studies will show significant diminution of

Fig. 1: CT scan with contrast shows a hypolucent area interdigitating with the cortex in the left frontal lobe. Partial obliteration of the left frontal horn and midline shift are noted. No mass lesion is visualized in this cut. Differential diagnosis includes vasogenic edema and cerebritis.

the affected area 12 to 24 hours after steroid therapy has been started. A disproportionately large amount of such edema around a well circumscribed round tumor highly suggests metastases; specially if it causes less significant ventricular distortion than that expected with a malignant glioma[8].

The configuration of the tumor per se, is characteristic. Most metastases have either a nodular or ring aspect (Fig. 2). Irregular margins with an ameboid contour is suggestive of glioma (Fig. 3). CT scan appearance, however, is unrealiable in further specifying the histological diagnosis. Only in certain cases can such a correlation be implied,[7 18 19] for example: vascular or cellularily dense tumors like melanomas, renal carcinoma, angiosarcoma, thyroid carcinoma and chorionic carcinoma give as a rule high coefficients of absorption. Of these, only melanoma occurs in significant numbers. The diagnosis of melanoma is further suggested when an intracerebral hemorrhage occurs concomitantly.

Massive intracraneal bleeding is a rare complication of gliomas (3.7 percent of patients) and it produces a stroke-like symptomatology less often (0.8 percent of patients).[20] Although statistical data are missing, it has been suggested to occur much more commonly in metastases.[21] Its detection is important as radiotherapy is contraindicated in hemorrhagic lesions. Survival after the onset of neurologic symptoms is usually short. Calcification, on the other hand, are rarely if ever seen in metastases and should be considered characteristic of primary brain tumors.

Tumor size may also serve as a differentiating factor between metastases and gliomas. A large recent series of metastases[2] revealed their range to vary from 9 to 96 mm along their longest length. Secondary brain tumors are therefore relatively small when compared to the average glioma. It could be presumed that the short survival of patients coupled to the counter-pressure exerted by the brain to an expansive

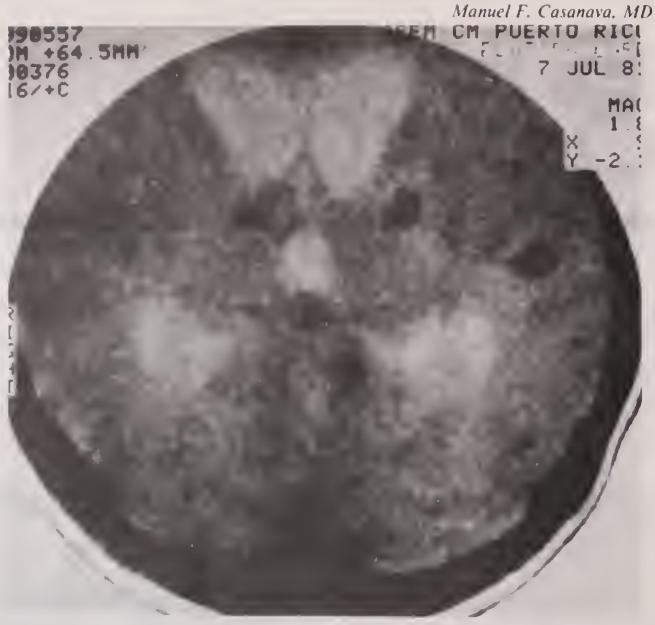

Fig. 2 CT scan with contrast in a patient with breast metastases shows multiple small round lesions. Obstructive hydrocephalus is noted.

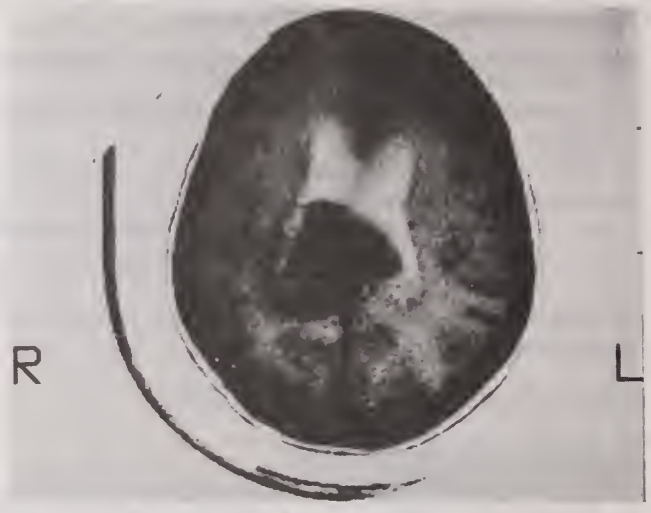

Fig. 3 CT scan with contrast shows an amorphous mass extending across the splenium of the corpus callosum. The varigated appearance and its avidity for white matter suggests a glioblastoma multiforme.

mass (which should be greater than to an infiltrative growth, as in gliomas) would limit the tumor size in case of metastases.

It would be unjust to finish the article without mentioning the role of the history, neurological examination and other complementary methods in the diagnosis of patients with metastases. Severe headaches, progressive paresis of the extremities, a change in character, convulsive crises and language disorders in a person with a primary neoplasia should alert the physician as to the possibility of metastases[22]. Prior excision of a skin lesion would suggest a melanoma. A stroke in a normotensive woman especially if oriental and in the reproductive age, should make the clinician aware of the possibility of metastatic choriocarcinoma,[23] while a similar history in a male patient with hematuria and back pain would call to mind a hypernephroma.

An abnormal neurological examination is usually the best screening procedure for deciding when to do a CT scan in patients with a primary neoplasia. In their study M.G. Dupont, et al[2] found that all patients suffering from cerebral metastases had an abnormal neurological examination. Contrariwise, the CT scan was negative in 22 patients who

presented a generalized cancer but had no neurologic symptomatology.

CT scanning is not the panacea of metastases detection. False-negative results do occur. It may be wise in such patients where clinical suspicion is high, to employ other diagnostic tests. Radionuclide scanning for example, may give abnormal or suspicious results under such circumstances in a significant number of cases[24]. Arteriography is less useful, as only 50 percent of metastases show varying degrees of vascularity and even when present, it may be difficult or impossible to distinguish from glioma, meningioma or abscess.[25] EEG may show periodic lateralized epileptiform activity early in rapid growing metastatic tumors; however, the main finding is usually that of polymorphic delta activity. The latter type of activity is seen with other focal intracerebral destructive lesions and unless two or more such foci are found, there would be no basis by EEG alone to suggest metastases.[26]

Resumen: Características por tomografía computarizada que en conjunto favorecen el diagnóstico de metastasis sobre el de tumor primario de cerebro:

1. **Más de una lesión.**
2. **Localización entre la unión de la materia blanca y gris.**
3. **Aspecto nodular o de anillo.**
   (a) **Una cantidad desproporcionada de edema vasogénico.**
   (b) **Una disminución significativa en el tamaño de la edema dentro de las primeras 24 horas de empezar el uso de esteroides.**
5. **Localización en un adulto de tumor en fosa posterior.**
6. **Evidencia de hemorragia intracranial.**

Características que desfavorecen el diagnóstico de metastasis:

1. **Cualquier edema que no sea vasogénico**
2. **La presencia de calcificaciones.**
3. **Un tumor de más de 100 mm. de largo a través de su mayor eje.**

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Premature Thelarche and Ovarian Cyst Probably Secondary To Estrogen Contamination

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Summary: **Three hundred and twenty two cases of premature thelarche have been reviewed. Thre was association to ovarian cysts in 13% of the cases, ten with elevated estrogens. The high prevalence of these conditions may be indicative of estrogen contamination. The association of premature thelarche with follicular ovarian cysts has rarely been reported. We postulate that the development of the cysts is secondary to a prolonged exogenous estrogen stimulation related in some instances to a genetic predisposition to estrogen hypersensitivity.**

Premature thelarche consists of the development of breast tissue in girls before eight years of age. The published incidence of these conditions in the U.S. is the experience of two large clinics with forty patients in a 10 years study period[1]. The frequency of premature thelarche among Puerto Rican girls observed during the last ten years has alerted us to investigate its newer and perhaps unique clinical aspects. A much higher incidence is probable inasmuch as those patients seen at the Puerto Rico Medical Center during the years 1972 to 1977 are not included herein. However, the number of cases seen at the latter institution is of real concern to one of the authors. Our interest is further enhanced by the alarming peak indicence in our island during the last three years. (Table I), a fact also noted by other pediatric endocrinologists and pediatricians.

Considering that the ingestion of exogenous estrogens may have been the cause of this increasing prevalence, a revision of all our cases was mandatory. This has been confirmed by others[2 3 4] after the ingestion of exogenous estrogens. Studies on the environmental estrogen contamination in our midsts are being conducted by pertinent authorities following our suggestion. It must be emphasized that the concurrent and unique increased incidence of ovarian cysts (13%) at the early ages of 8 months to 7 years, so clearly demonstrated in our sample besides other clinical findings, has prompted us to report on our experience.

TABLE I

Increasing Number of Patients with Premature Thelarche with Corresponding Years.

1982 (January)	4
1981	82
1980	89
1979	56
1978	29
1977	17
1976	0
1975	7
1974	7
1973	22
1972	9
Total	322

Materials and Methods

During the last ten years 322 cases of premature thelarche have been referred to the private practice of two pediatric endocrinologists by concerned pediatricians. Of the 322 cases, 256 (80%) were seen from 1978 to 1981. If the only significant physical finding at the initial evaluation consisted exclusively of breast enlargement, no studies were performed but a modification of the diet was advised and the patient was reevaluated within three months. This modification consisted of avoiding the use of local whole milk, poultry and beef. Those cases that had pigmentation of the areola, labia minora, signs of estrogenization of the vaginal mucosa and mucous vaginal discharge, were submitted to the following tests: total estrogens, bone age, skull roentgenograms, pelvic sonograms and urine FSH and LH. Gonadotropin levels were performed by radioimmune assay and the values obtained were compared with those reported by others in normal prepubertal females.[5 6 7 8 9 10] Estrogen levels in urine were determined by the method of McAnally and Hausman (normal values under 5 mcm per 24 hrs. in preadolescent and infant girls).[11] Whenever in infant girls a 24 hours urine collection was not feasible, serum samples of gonadotropins and estrogens were taken. Radioimmune assays determinations were used for the serum samples.

Geographic Distribution:

Premature thelarche and ovarian cysts were higher in the referrals from the metropolitan area of San Juan, 226 cases. A much lower incidence was noted in the patients referred from the mountainous region of the island: Barranquitas, Aibonito, Cayey, Jayuya (4 cases). The rest of the cases (92) were from different towns of the island.

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Age Distribution:

The greatest incidence of premature breast development was observed in the 6 to 24 months age group (198 cases) followed by 57 cases (18%) in the 49 to 72 months age group (Table II).

TABLE II

Age Distribution	
Age (Months)	Number of Patients
6 - 24	198
25 - 48	57
49 - 72	40
73 - 84	27

Results

Gonadotropins and estrogens were obtained in 75 (23%) of the 322 patients with premature breast development. In all instances, FSH and LH values were found normal. An elevation of estrogen levels was found in 15 patients, ten of whom had ovarian cysts. Sixty pelvic sonograms were performed and 41 showed ovarian cysts either unilateral, bilateral or multicystic. (Fig. 1). Controlled cases of pelvic sonograms matched for age and sex were negative for ovarian cysts. Accelerated bone age was present in 26 of the total number of cases. Only five patients with ovarian cysts and elevated estrogen had an accelerated bone age. The above data is summarized in Tables II, III and IV.

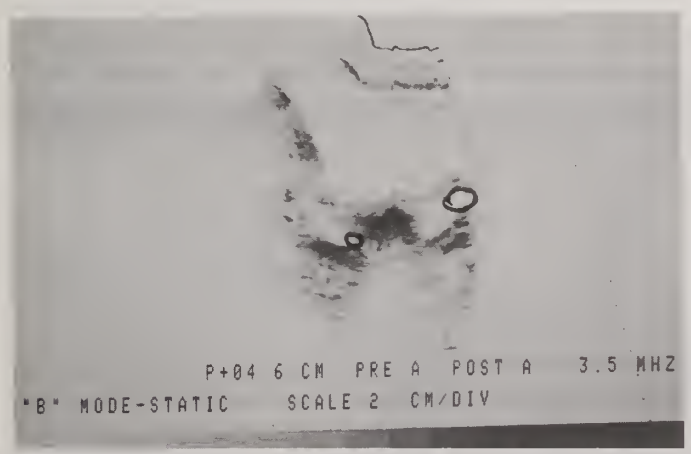

Fig 1. Pelvic Sonogram. A transverse view 4.6 cms. above xymphisis reveals enlarged left ovary measuring 4 x 2.5 cms. with a 1.5 cm. cyst. Right ovary measures 2 x 2 cms. with a 0.5 cms. cyst.

The detailed analysis of histories on all our patients, discards their use of medications or creams containing estrogens, and none had neurological or other adrenal disorders. There was no evidence of hypothyroidism in these cases, which eliminates the possibility of the multicystic ovaries reported in preadolescent girls with thyroid deficiency.[12] It was clearly observed in 97% of the cases that the appearence of abnormal breast tissue was probably related to the weaning of a formula to local whole milk in the infant group. At a later age, a dietary history of a greater consumption of local whole milk, poultry and beef was referred by the parents.

TABLE III

Data Distribution	
Total number of cases	322
Studied with Gonadotropin and Estrogen Assays	75
Abnormal Gonadotropins	0
Elevated Estrogen Levels	15
Ovarian cysts	41
Ovarian cysts and elevated estrogens	10
Accelerated bone age	26
Accelerated bone age and ovarian cysts	5
Accelerated bone age, ovarian cysts and elevated estrogens	5

In 87% of the cases significant involution of breast tissue was observed about 3 months after a diet modification. Some of the patients whose diet was not changed had concomittant ovarian cysts.

In a significant number of cases (42%) a positive family history of ovarian cysts was confirmed in their elder relatives, suggesting a genetic predisposition in the development of the ovarian pathology, possibly associated with a higher sensitivity to exogenous estrogens.

Ovarian cystectomies were performed in 31 of the patients. Pathological reports were consistent with follicular cysts of the ovary (Fig. 2,3) in all but one, where an ovarian fibroma was found.

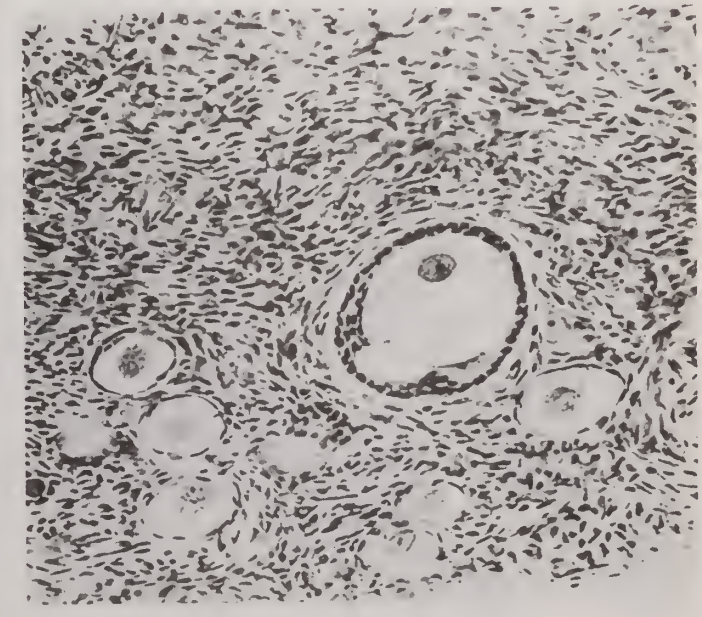

Fig. 2. Microsection of the ovarian cortex showing richly cellular stroma containing abundant primordial follicles and an almost mature graafian follicle. Cumulus oophorus is not visualized at the level section.

TABLE IV

Patients With Ovarian Cysts and Elevated Estrogens

Patient	Chronological Age	Bone Age	Estrogens	Vaginal Smears*	Pelvic Sonogram	Ovarian Cyst	Tanner Stage +	Vaginal Bleeding
C.C.	9 months	2.5 yrs.	15 mcg%	Not done	Done	+	II	No
C.A.	11 months	11 months	21 mcg%	62%	Done	+	II	No
M.C.	12 months	12 months	17 mcg%	45%	Done	+	II	No
C.G.	12 months	12 months	18 mcg%	60%	Done	+	II	No
M.C.	12 months	12 months	18 mcg%	52%	Done	+	III	No
G.M.	18 months	3.5 yrs.	8 mcg% (serum)	Not done	Done	+	II	No
M.R.	3 yrs.	6 yrs.	60 mcg%	72%	Not Done	+	II	Yes
S.N.	4 yrs.	6 yrs.	22 mcg%	66%	Done	+	III	No
M.A.	5 yrs.	5 yrs.	150 mcg%	70%	Not Done	+	III	No
A.R.	6 yrs.	10 yrs.	42 mcg%	62%	Done	+	II	Yes

* Normal percentage of superficial cells prior 8 years. is 0%.
From Kaufman, RH and Leeds, LJ: Cervical and vaginal cytology in the child and adolescent. Pediat Clin NA 19: 547, 1972.

\+ From Marshal, WA and Tanner, JM: Variations in pattern of pubertal changes in girls. Arch Dis Childh 44: 291, 1969.

Discussion

This paper presents a new clinical aspect of premature thelarche which presumably has been considered a benign condition[1]. Our findings disclosed a 13% concurrent and not ubiquitous association with ovarian pathology. The early diagnosis of the latter associated finding was suggested by pelvic sonography and in some by elevated estrogens.

The precocious development of isosexual characteristics in girls may be caused by: (1) Idiopathic or cerebral precocious puberty (2) An ovarian neoplasm, unusual in the overall experience of large clinics (3) Feminizing adrenal tumors, a very rare cause of estrogen excess and (4) Accidental ingestion or exposure to estrogen mimicking the appearance of endogenous excessive production of these sex steroids.[2 3 4]

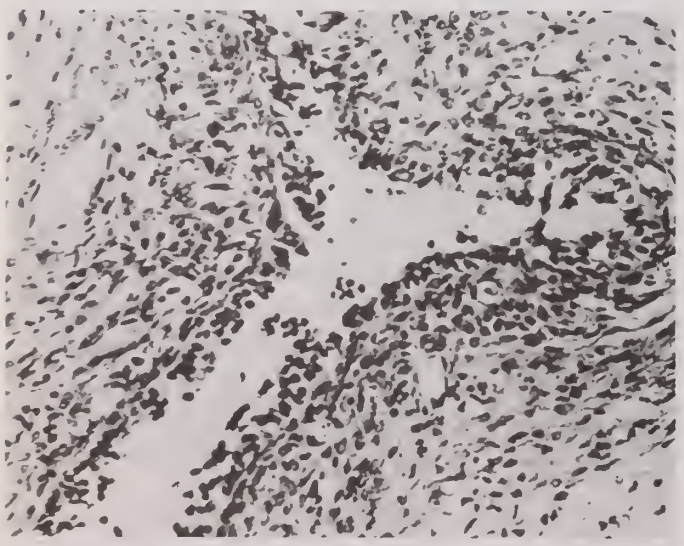

Fig. 3. Microsection of the ovarian cortex biopsy. Note the collapsed cystic formation in the ovarian cortex lined interiorly with cuboid and columnar cells, layered in places. At the periphery of the cyst intermingled cells of the theca folliculi can be identified. x 225-

Benign ovarian cysts may be found in premenarchal ovaries[13], but very rarely do they secrete sufficient estrogen to stimulate a precocious development of secondary sexual changes.[14] A review of the literature for the last ten years fails to reveal the association of follicular ovarian cysts to premature thelarche.

Further support to our conclusions is obtained from studies in the human and other mammals showing that in spite of low concentrations of gonadotropins, increasing concentration of estrogens may stimulate ovarian follicular growth.[15] We believe that in those patients with normal estrogen levels, serial samples would have been more informative. Unfortunately, these could not be done in our patients because the assay is very expensive.

Since isosexual pseudoprecocious puberty may be associated with malignant cysts[16 17] ovarian cystectomy was performed in 31 patients, some preceded by laparoscopy. The justification for surgery was based on the fact that a resectable ovarian neoplasm may be the cause of the precocious sexual development. In some of our patients, the ovarian cyst was autonomous and vaginal bleeding was present. Fortunately, we have no malignant neoplasm reported in the group submitted to ovarian cystectomy.

At the present time, we are very closely following ten girls under 4 years of age who have ovarian cysts identified by sonogram. In order to study the natural course of this disease, no surgery has been performed in these patients. Parental consent was obtained for these observations and all studies will be repeated every six months.

After exclusion of an endocrine etiology, we strongly suspect that the high incidence of thelarche and ovarian cysts observed in these series has resulted from a continous and prolonged exogenous estrogen stimulation.

The identification of the exogenous source of estrogens acquires more importance considering that this substance induces premature development of secondary sexual characteristics in females, gynecomastia in males and is a carcinogenic agent. Another side effect is the premature

closure of the epiphysis resulting in short stature, an unpleasant feature for our developing population. The contents of this study and the increasing incidence during the last three years justifies our petition to the Medical and Veterinary professions, as well as our Executive, Legislative and Judicial power, to enforce the necessary laws prohibiting the use of all estrogen derivatives and estrogen-like substances in cattle an poultry to promote their growth.

Addendum

Since the preparation of this manuscript, estrogen substances and derivatives have been found to be available for use by our local cattle industry. A strong suspicion that these same agents may be contaminating other type of meats is under investigation.

In the issue of March 27, 1982 of The Lancet, the editor comments on the use and misuse of anabolic agents in meat production. The W.H.O. Committee on Food Additives in currently reviewing the acceptable use of anabolics in meat.

Resumen: Se han revisado 322 casos de telarquia precoz. En un 13% de los casos hubo asociación a quistes de ovario, en 10 de estos casos se demostraron niveles de estrógenos elevados. La alta incidencia de estas condiciones puede ser indicativo de contaminación por estrógenos. La asociación de telarquia precoz con quistes foliculares de ovario ha sido reportada en muy pocos casos. Postulamos que el desarrollo de los quistes es secundario a un estímulo prolongado de estrógenos, posiblemente relacionado en algunos casos, a una predisposición genética de hipersensitividad a estos esteroides.

Acknowledgments

The authors wish to acknowledge the invaluable cooperation of Dr. José E. Taveras, Chief of the Department of Pathology, De Diego Hospital, for the pathological reports and illustrations of this paper.

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"Heavens, no, I'm not Tarzan. I'm his answering service."

(Reprinted from Playboy)

BILIARY ATRESIA:
A Clinical Review

Pedro Rosselló, MD

Abstract: We reviewed the cases of biliary atresia managed at the University and University Children Hospitals during a recent 10 year period. Sixteen patients were identified from computer listings; of these 13 records were located and reviewed. The presenting signs and symptoms for these cases were similar to those described in the literature. The hospital work-up routinely included bilirubin and liver function tests in all patients, but other more specific studies were only sporadically performed (T.O.R.C.H. titers, liver scan). There were no preoperative transcutaneous liver biopsies performed. The surgical treatment in cases with uncorrectable type of biliary atresia consisted of an exploratory laparotomy and liver biopsy, with a cholangiogram if possible. All patients with uncorrectable type of biliary atresia followed a documented downhill course with eventual death. The age at operation was relatively late, occurring at an average of 15 weeks. In view of present evidence that biliary drainage, a jaundice-free state, and possible long term survival are attained in a significant percentage of babies with uncorrectable biliary atresia, and in view of the clear correlation between succesful drainage and early operation, it is recommended that infants with jaundice unresolved after one month, undergo an expeditious diagnostic work-up and subsequent early reconstruction with a Kasai type procedure before the age of 8 weeks.

Biliary atresia is an uncommon disease of unknown etiology and obscure pathogenesis, associated with an unusually high mortality. Traditionaly this entity has been regarded as a non-curable condition. However, approximately 10-25% of cases have been described as "correctable", meaning that these are amenable to surgical bypass reconstructions allowing for potential bile drainage. The remaining have been considered "uncorrectable", due to the absence of extrahepatic ducts in continuity with the liver. Some believe that irrespective of type, there are no longterm survivors for this condition, due to an ongoing process of cirrhosis.

Kasai reported an innovative approach to "uncorrectable" biliary atresia consisting of a hepatoportoenterostomy.[1] Using this type of technique reports of relatively longterm (greater than 5 years) jaundice-free survival are being published from various centers.[2 3 4]

We undertook to review the cases of biliary atresia seen and managed at the University and University Children's Hospital during the most recent ten year period, in an effort to define the clinical presentation, management and results of this condition in our environment.

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Methods and Material

A search for records with a diagnosis of biliary atresia, within the period of January 1969 to July 1980, was carried out. A listing of patients with this diagnosis was obtained from the research section of the Medical Record Department, Puerto Rico Medical Center. All patients with this diagnosis except for those in the period of April 1977 to April 1978 were included. The aforementioned one year period had not been coded, and therefore record research by diagnosis was not possible. Sixteen patients with biliary atresia were identified from the computer listings. Of these, 13 records were located and reviewed. The data from these form the basis for this report.

Results

I. *Clinical*

Of the 16 patients on record with the diagnosis of biliary atresia 9 were male (56%). All but two of these patients were admitted to the hospital at age 3 month or less. The exceptions were 5 and 8 months old respectively at the time of admission.

All patients except one, were admitted to the hospital with a primary presenting complaint of jaundice. Jaundice presented as early as the first day of life in some, and in most within the first week. Acholic stools were reported as part of the admiting signs in seven of thirteen (54%). There more other sporadic symptoms including vomiting,[2] dark urine,[1] abdominal distension[1] and diarrhea[1]. The liver was reported enlarged in seven of thirteen cases (54%); there was splenomegaly in three (23%); abdominal distension was reported in 2 (15%) and malnutrition in one (8%).

TABLE I

Clinical Findings

	Number	Percent
A. Presenting complaints		
Jaundice	17	100%
Acholic stools	7	54%
Vomiting	2	15%
Dark urine	1	8%
Distention	1	8%
B. Physical Signs		
Scleral or skin icterus	13	100%
Hepatomegaly	7	54%
Splenomegaly	3	23%
Abdominal distention	2	15%
Malnutrition	1	8%
C. Associated Congenital Anomalies		
Hypospadias	1	8%
Cardiovascular	1	8%
No associated anomaly	11	84%

There were 2 patients with associated congenital anomalies: hypospadias in one and cardiovascular anomalies in another. There was an additional child who presented with necrotizing enterocolitis. There were no associated congenital anomalies in 84% of the cases.

All these neonates had a preoperative biluribun of greater than 7.5 miligram percent. Of those 3 months or older at diagnosis, all except one had levels above 10. The fractionation of bilirubin between direct and indirect levels was not helpful diagnositically. Most of the direct bilirubin values fell between 40-60% of total bilirubin. Liver function text were performed in all patients. There were marked elevations of alkaline phosphatase, L.D.H. and S.G.O.T. in all. The magnitude of elevation did not appear to correlate with the age of the patient. T.O.R.C.H. titers (toxoplasmosis, rubella, cytomegalovirus, herpesvirus) were not routinely performed except in some recent cases. There were no positive titers reported. There was one case with a positive V.D.R.L. in the mother and child. A Rose Bengal liver scan was done in three children, and a Technitium - 99 scan or a gold scan were performed each in one case. All showed no excretion and increased uptake consistent with biliary atresia. There were no preoperative transcutaneous liver biopsies performed. Twelve of the patients were operated and had open liver biopsies. The remaining case died before operation. The biopsies were reported as showing biliary cirrhosis, cholestasis, proliferation of bile ductules, and all were interpreted as consistent with biliary atresia.

TABLE II

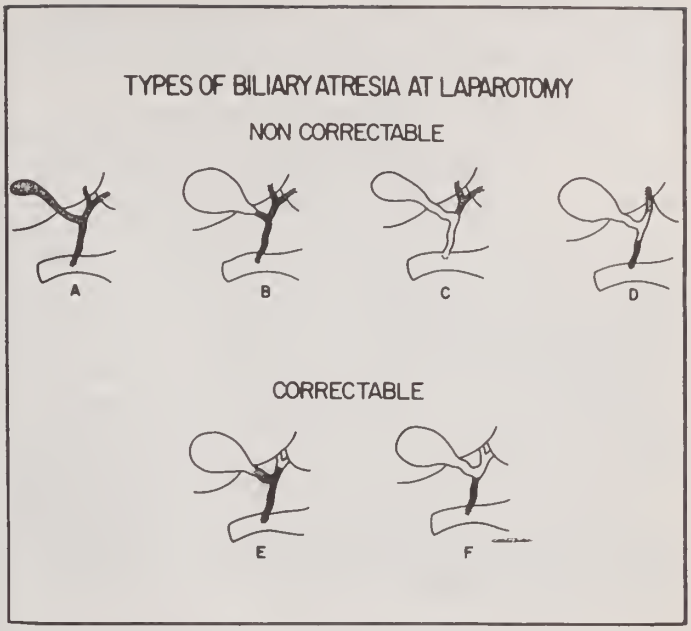
Diagnostic Studies

	Number	Percent
1. Bilirubin 7.5	13	100%
2. L.D.H., abnormally elevated	13	100%
3. S.G.O.T., abnormally elevated	13	100%
4. Alkaline phosphatase, abnormally elevated	13	100%
5. T.O.R.C.H. Titers, positive (N×3)	0	0%
6. Liver Scan (N×5), Positive	5	100%
Rose Bengal (N×3)	3	100%
Tecnitium	1	100%
Gold	1	100%

II. *Treatment*

A. Operative Findings

There were twelve infants who underwent an exploratory laparotomy. The findings described included: A) no evidence of gallbladder or biliary duct;[3] B) hypoplastic or atretic gallbladder without ducts;[5] C) a patent gallbladder with complete proximal atresia;[1] D) a dilated common duct and gallbladder separated by segments of atresia proximally and distally.[1] All these ten cases presented the classic findings of "uncorrectable" biliary atresia. One case presented with a dilated common duct in continuity with the liver, with distal atresia, and a separate dilated gallbladder. E) The remaining child had a dilated common duct and gallbladder with distal atresia. F) These last two were the only cases found with a "correctable" situation.



B. Operative Procedures

There were twelve opeative procedures. Four patients had an exploratory laparotomy with a liver biopsy; five had an exploratory laparotomy liver biopsy and cholangiogram. One patient with a patent gallbladder and with distal obstruction underwent, in addition to the exploratory laparotomy and liver biopsy, a cholecystostomy. In one patient a choledocho-duodenostomy was performed between a dilated common duct (which showed no connection with hepatic radicles) and the duodenum. The final patient, with a dilated common duct in continuity with liver bile ducts, had a choledocho-duodenostomy.

TABLE III

Operative Procedures

	Number	Percent
Laparotomy, Liver biopsy	4	33%
Laparotomy, Cholangiogram, Liver biopsy	5	42%
Laparotomy, Cholangiogram, Liver biopsy, Cholecystomostomy	1	8%
Choledochoduodenostomy	2	17%

C. Treatment Results

Three patients died during follow-up at the University Hospital; one at two month of age (sepsis); another at 34 months (GI bleeding); and the last at 42 months (GI bleeding). Nine patients were alive at the time of the last follow-up visit at the University Hospital, with an age ranging from four month to twenty five month. These children were either lost to follow-up or transfered to regional or local health facilities for terminal care. All had a documented deteriorating condition: three had episode of GI bleeding, two episodes of sepsis and five ascites and hepatomegaly. The child with the correctable type of biliary atresia who had a choledocho-duodenostomy, after a short period of follow-up appeared stable and jaundice-free.

There was no persistent drop in bilirubin in any of the

cases of non-correctable biliary atresia. The case with the correctable type of atresia showed a gradual lowering of bilirubin after discharge from the hospital.

TABLE IV

Mortality, Morbidity*

		Number
Dead (Range 2 mo. - 40 mo.)		
Deteriorating (follow up 4 mo. - 25 mo.)		9
GI Bleeding	3	
Sepsis	2	
Ascites	5	
Stable		1
Total		13

* Mean age at operation 15 weeks.
Median age at operation 12 weeks.

Ten of the cases had no evidence of bile excretion as measured by a decrease in th serum bilirubin level or by detection of urobilinogen in the stool. The one case which had a cholecystostomy for distal common duct obstruction evidenced daily drainage through the tube of 100 to 120 cc of bile. The patient died six week postoperatively secondary to the complications of necrotizing enterocolitis, bowel perforations and sepsis. The level of bilirubin had decrease from over 20 milligram percent preoperatively to 8.5 postoperatively.

D. Age at Operations

These infants were operated at ages ranging from six weeks to ten month. The mean age of operation was 15 weeks and the median age 12 weeks. The two cases which seemed to have a potentially reconstructable situation appeared at the early end of the age spectrum: the child having a common duct in communication with a gallbladder (operated at six weeks) and the "reconstructable" case with a dilated common duct (operated at nine weeks of age).

Discussion

Biliary atresia exists when there is absence or non-patency of the extrahepatic biliary ducts. It is estimated to occur in approximately 1:25,000 live births. There appears however to be a national or ethnic variation in the incidence being more commonly reported in Japan than in the U.S.[4] In Puerto Rico we have no accurate records of the true incidence of this condition, although it's low frequency is confirmed by our finding of only 16 cases, over a period of 10 years, managed at a large Pediatric referral center.

The specific etiology is unknown, although the pathogenesis appears to be that of a progressive intrauterine or neonatal sclerosing cholangitis.[3] There is evidence to suggest that during the early phases of the disease there are patent intrahepatic ducts extending from the liver periphery to the area adjacent to the porta hepatis. These findings form the basis for the modern therapeutic approach to this previously hopeless condition.[1] The inflammatory process however, appears to be progressive, underlining both the need for early intervention to secure bile drainage and the inevitably irreversible nature of the cirrhotic process in some cases.

As derived from our reviewed cases, these children may present with jaundice as early as the first days of life. In this group there appears to be a delay in undertaking and completing a diagnostic work up, and in following this with an exploratory laparotomy. The mean age at exploration was 15 weeks. Based on national U.S. and Japanese experience it is recommended that this diagnostic work up be completed by the 6th week of life, in order to allow for exploration and operative cholangiogram by the 8th week.[3] [4] An early preoperative diagnostic battery should include: a liver scan; an ultrasound study of the portal area in research for cysts or masses; serum studies (bilurubin levels; liver function tests; toxoplasmosis, rubella, cytomegalic virus, and herpes virus titers; hepatitis antigen and alpha -1- antitrypsin determinations) urine and stool determinations for urobilinogen and bile. In our reviewed cases, bilirubin levels, enzyme studies were routinely done, but the T.O.R.C.H. titers, the ultrasound, and liver scans were only sporadicaly performed. Recently imidoacetic scans of the liver have been preferentially advocated over the traditional Rose Bengal Scans, because of the agent's closer behavior to bilirubin uptake and transport.

The importance of these diagnostic tests is to determine a possible cause for the neonatal jaundice. Usually no definite cause is identified, and the tests are only consistent with a picture of cholestatic jaundice. An exploration with operative cholangiogram is then indicated. In addition to biliary atresia, the surgical differential diagnosis in non-resolving jaundice includes biliary hypoplasia, inspissated bile syndrome, choledochal cyst, Caroli's disease, and perforation of the extrahepatic bile ducts.[4]

Exploration includes an operative cholangiogram (when possible), liver biopsy and possible exploration of the portal area. Biliary atresia, if found, can be of a "correctable" or "uncorrectable" type, depending on whether or not there are gross patent extrahepatic ducts in continuity with the intrahepatic duct system. Approximately 10-25% of cases are of the correctible type.[4] We found two cases amongst 13 (15%). The surgical approach in these cases involves the creation of a biliary enteric connection for bile drainage, usually a choledocho or cholecystojejunostomy in a Roux — en— Y fashion.

All cases without grossly patent extrahepatic ducts in continuity with the liver are classified as "uncorrectable". In this series there were 10 such cases. All of these underwent only a diagnostic operative procedure, combining a cholangiogram, liver biopsy, and portal area exploration. These cases were followed until death or were refered to local health facilities following a progressively downhill course with hepatomegaly, ascites, and episodes of gastrointestinal bleeding or sepsis.

Kasai reported an ingenious technique for the treatment of these incurable "uncorrectable" cases.[3] Based on histologic findings of microscopically patent bile ducts at the porta hepatis, he advocated creation of an hepatic portoenterostomy connecting a loop of bowel to a previously dissected porta hepatis. In this series of 89 patients he reported bile flow in approximately two thirds, with total dissapearance of jaundice in one third.[2] These results have improved in recent years with a jaundice free state achieved in

61%. Active bile flow after surgery is related to the age at operation. More than 90% of patients operated under 60 days of age show excretion whereas none of those over 120 days drained bile. Kasai's series now includes 19 patients with jaundice-free five year survival.[2]

Similar experiences with the Kasai opeation or one of its several modifications have been reported from other Japanese institutions. Established bile excretion occurs in two thirds and complete clearing of jaundice in one third of cases with "uncorrectable" biliary atresia. Rates for five year jaundice-free survival are 25-30%.[3] A similar picture is now emerging in the reported cases from the U.S. However, the most important single factor determine success in bile drainage remains the age at operation: approximately a 50% rate of bile drainage if operated before 3 months, 80% in those intervened before 8 week of age.[4]

TABLE V

Non Correctible Biliary Atresia

	Exploration (UDH)	Kasai Type Procedures
Active Biliary Excretion	0	60%
Jaundice Free State	0	40%
Jaundice Free 5-Year Survival	0	25-30%
Longest Survivors	3-4 Years	23-25 Years

In view of the present evidence that bile drainage, a jaundice-free state, and possible longterm survival are attained in a significant percentage of babies with this "uncorrectable" biliary atresia (table V), and in view of the clear correlation between succesful drainage and early operation, we believe that a more aggressive aproach should be followed in these patients. This involves early diagnostic work-up in infants with unresolved jaundice after one month, and early reconstruction with a Kasai type procedure, ideally before 8 weeks of age. At the present time only in this manner may we hope to alter the dismal outlook of this condition in our local environment.

Resumen: Hemos revisado los casos de atresia biliar manejados en los hospitales Universitario y Universitario de Niños durante la más reciente década. Se identificaron 16 casos por listado de computadora; se pudieron recobrar y revisar 13 de esos expedientes. Los síntomas y signos de presentación son similares a los descritos en la literatura. El trabajo diagnóstico intrahospitalario incluyó rutinariamente niveles de bilirubina y funciones hepáticas, pero otros estudios más específicos solo fueron llevados a cabo esporádicamente. No se tomaron biopsias transcutaneas preoperatorias. El tratamiento quirúrgico de los casos de atresia biliar no corregible consistió en una laparotomía exploratoria con biopsia hepática, y en ocasiones un colangiograma intraoperatorio. En todo caso de atresia biliar no corregible se documentó un cuadro de detrioro progresivo. La edad promedio cuando se efectuó la intervención quirúrgica fue relativamente avanzada, 15 semanas. Debido a la evidencia acumulada en la literatura que demuestra que se puede obtener drenaje biliar, un estado libre de ictericia y sobrevida a largo plazo en un porciento significante de casos con atresia biliar no coregible, y debido a que se ha demostrado una correlación clara entre la intervención quirúrgica precoz y el éxito de esta, recomendamos que en aquellos infantes que demuestren ictericia persistente durante el primer mes de vida, se practiquen las intervenciones diagnósticas rápidamente y se sometan a una reconstrucción temprana con un procedimiento tipo Kasai, antes de las 8 semanas de edad.

Acknowledgements:

We would like to thank Alfredo Piñero Pereira, a medical student summer fellow (1980) in our laboratory, for assistance in compling the data for this study; to the personell of the Research Section of the Medical Research Department, P.R. Medical Center for assistance in obtaining the records; to Laura Mercado for help with the manuscript; and to Carlos Marin for the artwork involved.

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The Immunocompromised Patient: Guidelines for the Clinical Approach

C.H. Ramírez-Ronda, MD, FACP
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The clinical, diagnostic, and therapeutic approach to infections in immunocompromised patients is complicated by the fact that these patients are critically ill, immunosuppressed and have rapidly progressive clinical courses. The multiple physicians involved in their care are not always in communication, which unfortunately delays major decisions regarding management. For this reason, the Infectious Disease specialists at Stanford University and our own program try to insure that one physician is ultimately responsible for, and coordinates the care of these critically ill patients. In addition, we consider the team approach to be optimal, but recognize that certain members of the team may not always be available. In his event, alternate physicians must be available. The necessity of having the appropriate technical and medical-surgical facilities had led a number of authors to recommend that these patients be cared for solely in major medical centers whenever possible. This necessity has unfortunately altered the quality of life for many patients in an untoward manner, especially where they have

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TABLE I

Examples of Immune Defects and Common Pathogens in Patients with Malignancy

Neoplastic Disease	Immune Defect	Associated Pathogens	
Acute nonlymphocytic leukemia	Phagocyte (PMN)	Bacterial:	*Staphylococcus aureus* Gram-negative bacilli, especially *Pseudomonas aeruginosa*
		Fungal:	*Candida spp., Aspergillus spp.*
Hodgkin's disease Hairy cell leukemia	CMI	Bacterial:	*Listeria monocytogenes* *Nocardia asteroides* *Pseudomonas aeruginosa* *Salmonella* species *Mycobacterium* species
		Fungal:	*Cryptococcus neoformans* *Candida* species *Coccidioides immitis* *Histoplasma capsulatum*
		Protozoal:	*Toxoplasma gondii* *Pneumocystic carinii* *Strongyloides stercoralis*
		Viral:	Herpes simplex, Varicella-zoster, Cytomegalovirus
Chronic lumphocytic leukemia Multiple myeloma	HI	Bacterial:	Pneumonococci *Hemophilus influenzae* Gram-negative enteric bacilli
			Pneumocystic carinii

Adapted from: Sotman, et al. Am. J. Med. 69:814-818, 1980
Mackowiack, et al. Am. J. Med. 68:718-724, 1980
Schimpff, et al. Am. J. Med. 59:695-701, 1975
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Notter, et al. Rev. Inf. Dis. 2:761-800, 1980

had to move themselves and their faimilies to such centers.

The team may be rather extensive but most often consists of the patient's personal physician, housestaff, hematologist-oncologist, radiologist, infectious disease consultant, thoracic surgeon, laboratory microbiologist and patholigist. Coordination of such a team effort is not only a major responsibility but a necessity if these patients are to be cared for appropiately.

We will attempt to provide certain guidelines which we hope will be helpful for physicians caring for such patients. For this reason the reader is referred to the bibliography for critical articles related to the subjects covered. What follows then will be a discussion, dealing with selected clinical, diagnostic and therapeutic considerations which the practicing physician may use in dealing with infections in high risk patients, primarily those with hematologic malignancy receiving high dose immunosuppressive drugs, including corticosteroids.

I. Clinical and Diagnostic Approaches

In the approach to the immunocompromised patient with suspected infection, it is helpful to have at least a superficial understanding of the immune defects associated with the patient's underlying disease and/or the drugs they are receiving since all of these factors may predispose to infection with a variety of bacteria, fungi, viruses, protozoa and helminths (Table I). The defects may be in humoral immunity, cell-mediated immunity (CMI) or both.

In normal individuals these two arms of the immune system may act alone or synergistically to both protect against and fight infection. It is important to recognize that these two arms of the immune system, often defend against different types of organisms. Thus in the patient with multiple myeloma who presents with pneumonia, we suspect pneumococci as the primary etiology, since the immune defect is a deficiency in normal quantities of circulating immunoglobulins (antibodies). Such antibodies are necessary for opsonization of pneumococci for phagocytosis and killing. In contradistinction, when a patient with Hodgkin's disease or hairy cell leukemia presents with pneumonia, the differential diagnosis includes certain of the facultative and obligate intracellular bacteria and fungi, defense against which is primarily cell-mediated. If these patients are also receiving cytotoxic agents and/or corticosteroids both humoral and cell-mediated immunity will be affected which thus will determine the etiology of the infection.

In dealing with infections in immunocompromised patients, clinicians must also be aware of the changing patterns and predominance of microbial isolates in their own hospitals. Certain epidemiologic factors may suggest the etiology of an infection in such patients. For instance, in certain institution, such as Stanford University Hospital, the incidence of Aspergillus species as a cause of serious infections in patients with acute nonlymphocytic leukemia is relatively high, whereas in other institutions it is rarely seen. Another example is the increasing number of nosocomial infections caused by *Legionella pneumophila,* which in certain centers is nine times more frequent in immunocompromised than in non-immunocompromised patients.

Some of the most common sources of nosocomial infections are indwelling intravenous lines, urethral catheters and respiratory care equipment. More recently tranfusion as a source of life-threatening infection other than hepatitis B and infection from contaminated foodstuffs has been

TABLE II

Nosocomial Pathogens in the Immunocompromised Host

Pathogens	Epidemiology		
	Endogenous	Exogenous	Device Associated
Bacterial	++	+	+
S. aureus	+++	...	+
S. Epidermidis			
Corynebacterium species	+++	...	+
Gram-negative rods	++	+	+
Fungal			
Candida species	+++	...	+
Aspergillus species	...	+++	...
Viruses			
Herpes simplex	+++	...	...
Varicella-zoster	++	+	...
Cytomegalovirus	+	++	+ (blood or white cell transfusions)
Protozoa			
Pneumocystis carinii	++	+	...
Toxoplasma gondii	++	+	...

Adapted from Young, L.S. Am. J. Med. 70: 398-404, 1981.

emphasized. Cytomegalovirus (CMV) infection acquired by transfusion or transplantation of a previously infected kidney has predisposed to serious infection and death in recipients. Colonization of the GI tract, the most common origin of the etiologic agents which cause life-threatening infection and death in patients with prolonged and severe granulocytopenia may occur when these patients are fed contaminated foods such as salads, which are known to contain significant numbers of Pseudomonas spp., Klebsiella spp., and *E. coli*. See Table II.

In addition to the clinical history, the physical examination of these patients must be complete, including careful examination of the fundi (e.g. for characteristic features of Toxoplasmic, CMV or fungal retinitis) and skin (e.g. for characteristic or suggestive lesions of icthyma gangrenosa due to *Pseudomonas aeruginosa; Candida tropicalis; Candida albicans; herpes Simplex* and *Herpes zoster.*) These two sites which are so frequently missed, are excellent "windows" which afford us an insight into the diagnosis of the infection. Any new skin lesions which cannot be easily explained to be due to durg eruption or bleeding diatheses, should be biopsied or scraped and appropriately stained to assist in the definitive diagnosis. See Table III.

TABLE III

Common Pathogens by Site of Infection in Immunocrompromised Patients

Site of Infection	Neoplastic Disease	Associated Pathogens
Oropharynx (including esophagus)	Acute nonlymphocytic leukemia	Bacteria: Streptococci *Staphylococcus aureus* *Pseudomonas aeruginosa* *Klebsiella pneumoniae,* *E. coli* Fungi: *Candida* species *Aspergillus* species Mucor Viruses: Herpes simplex
Central nervous system	Acute nonlymphocytic leukemia	Bacteria: Gram-negative bacilli (*Pseudomonas, klebsiella, E. coli*) Fungi: *Aspergillus* species *Candida* species Mucor
	Hodgkin's	Bacteria: *Listeria monocytogenes* Fungi: *Cryptococcus neoformans* *Coccidioides immitis* Protozoa: *Toxoplasma gondii* *Strongyloides stercoralis* Viruses: Varicella-zoster
Cutaneous	Acute nonlymphocytic leukemia	Bacteria: *Staphylococcus aureus* *Pseudomonas, Klebsiella, E. coli* Fungi: *Candida species, Aspergillus* species Mucor Viruses: Herpes simplex
	Hodgkin's	Bacteria: *Mycobacterium* species *Nocardia asteroides* Fungi: *Cryptococcus neoformans* *Histoplasma capsulatum* *Coccidioides immitis*

Table III (Cont.)

		Viruses: Herpes simplex Varicella-zoster
Pulmonary	Acute nonlymphocytic leukemia	Bacteria: *Staphylococcus aureus* Gram-negative bacilli (*Pseudomonas, Klebsiella, E. coli*)
		Fungi: *Aspergillus* species *Candida* species Mucor
	Hodgkin's	Bacteria: *Mycobacterium* species *Nocardia* asteroides
Pulmonary	Hodgkin's	Bacteria: ? *Legionella pneumophila*
		Fungi: *Cryptococcus neoformans* *Histoplasma capsulatum* *Coccidioides immitis*
		Protozoa: *Pneumocystis carinii* *Stongyloides stercoralis*
		Viruses: Herpes simplex Varicella-zoster Cytomegalovirus
		Other: *Chlamydia trachomatis*
	Chronic lumphocytic leukemia	Bacteria: Pneumococci *Hemophilus influenzae*
		Protozoa: *Pneumocystis carinii*

Adapted from Armstrong, D., Immunosuppressed Symposium - Elsevier - Holland.

The need for urgency in diagnosing infection in immunocompromised patients has been emphasized in clinical investigations of leukemic patients undergoing prolonged periods of granulocytopenia (≤ 1000 PMN/mm^3). In such patients, mortality approaches 40-50% and is significantly increased if the patient has bacteremia or pneumonia. A major predisposing factor to pneumonia in these patients is the fact that their oropharynx becomes colonized with enteric gram-negative bacteria. These bacteria are often nosocomial and therefore resistant to a variety of antimicrobial agents used in the hospital environment. Some general guidelines for the diagnostic approach to the febrile granulocytopenic patient are given in Table IV. These guidelines extend also to numerous other patient types in the growing legion of immunocompromised patients.

From the onset of fever to the time of death in the patients we are discussing here may be less than 24 hours. This is the rason for the organized and aggressive approach to the diagnosis.

Even in the nonimmunosuppressed patient, approximately 50% of bacteremic patients who die, die within the first 24 hours. Following the obtaining of blood cultures, cultures of orifices and body fluids and appropriate staining of these materials, the physician may still be left without a diagnosis. This may occur in as many as 30-40% of patients. A special case in point is the patient with pulmonary infiltrates, for it is in these patients that we have observed the most costly waste of valuable time in making a decision as to the next diagnostic procedure. This decision must be made with intelligence and restraint, with a complete knowledge of the etiology of these pneumonias and the invasive procedures available for their diagnosis. This decision must also be based upon a careful consideration of the complications, potential risks and benefits of such procedures and upon the impact such a decision will have on the patient's quality of life.

Transtracheal aspiration (TTA) is a logical first alternative since thre are few contraindications to its use and because it is a safe procedure if done by personnel familiar with the technique. If TTA cannot be done or is unsuccessful, more invasive procedures may be considered. The type of procedure and the urgency with which it is done in dependent upon the clinical assessment of the patient's course, the type and location of the pulmonary infiltrate, the presence of bleeding diastheses and upon the expertise available at a given institution for performing such procedures. In addition, the physician's decision to obtain a diagnosis by one of these invasive techniques, must also be weighed against the possibility that the cause of the pulmonary

TABLE IV

Some General Guidelines for the Diagnostic Approach to the Febrile Granulocytopenic Patient

I. Initial Evaluation

A. Through history and physical examination

1. Possible etiologies suggested by physical findings or site of infection
2. Fundoscopic exam
   a. Endopthalmitis:
      Aspergillus species
      Candida species
      ? Bacteria
   b. Chorioretinitis:
      Toxoplasma gondii
      Cytomegalovirus

B. Laboratory and diagnostic tests (minimum)

1. CBC with differential
2. Chemistry panel with creatinine
3. Urinalysis
4. Blood culture(s)
5. Chest x-rays (CXR)

II. Patient with Lung Infiltrate on CXR

A. Productive or induced sputum

1. Immediate examination of sputum by gram stain, acidfast stain

Culture for aerobes, fungi, mycobacteria

B. Failure to expectorate or induce sputum or obtain useful information from (A)

1. Consider invasive procedures in the following order:
   Transtracheal aspiration
   Flexible fiberoptic bronchoscopy with bronchial washings, brushings, and biopsy

C. Handling of pulmonary specimens obtained by invasive procedures
   Percutaneous needle aspiration and/or biopsy. Open lung biopsy

1. Immediate examination by:
   Gram stain, acid-fast stain and fungal wet mount (KOH)
   Gomori methenamine silver staining for pneumocystis
   Direct fluorescent antibody staining for *Legionella* or viruses if suspected
2. Culture for aerobes and anaerobes, mycobacteria, fungi; *Legionella* and viruses if suspected clinically

III. Patient Without Lung Infiltrate on CXR

A. No abnormal physical findings

1. Initiate empiric antibiotic therapy after peripheral culturing is completed

B. Skin or mucous membrane lesions

1. Obtain material by scraping, aspiration or biopsy
2. Examination of material by gram stain, fungal wet mount, acidfast stain, tissue stain for fungi, direct fluorescent antibody stain for herpes virus of suspected clinically
3. Culture for aerobes and anaerobes, fungi, mycobacteria, viruses if suspected

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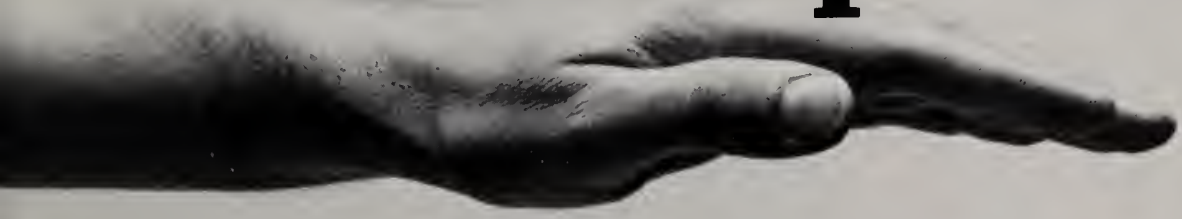

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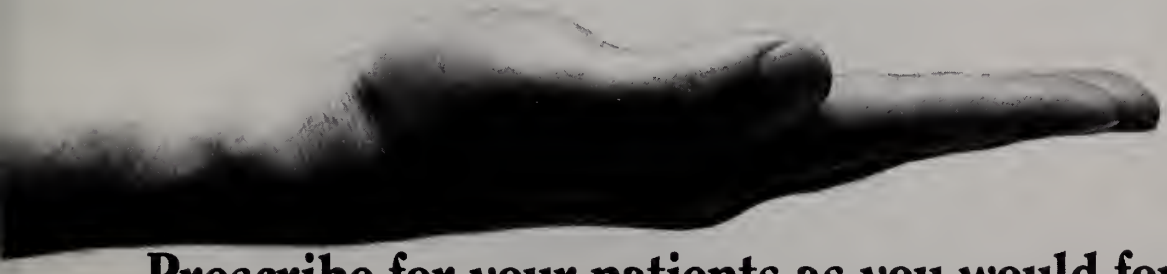

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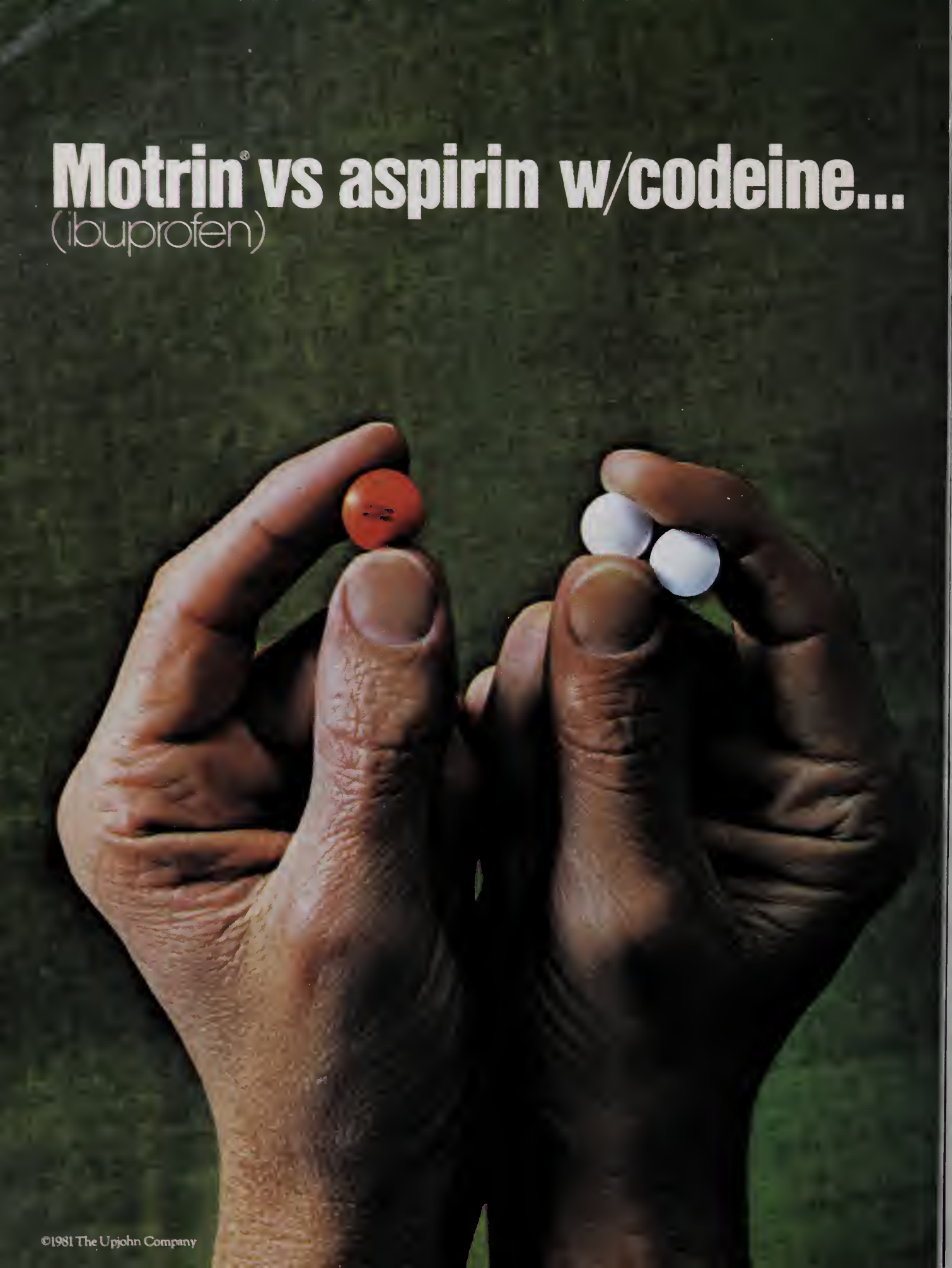

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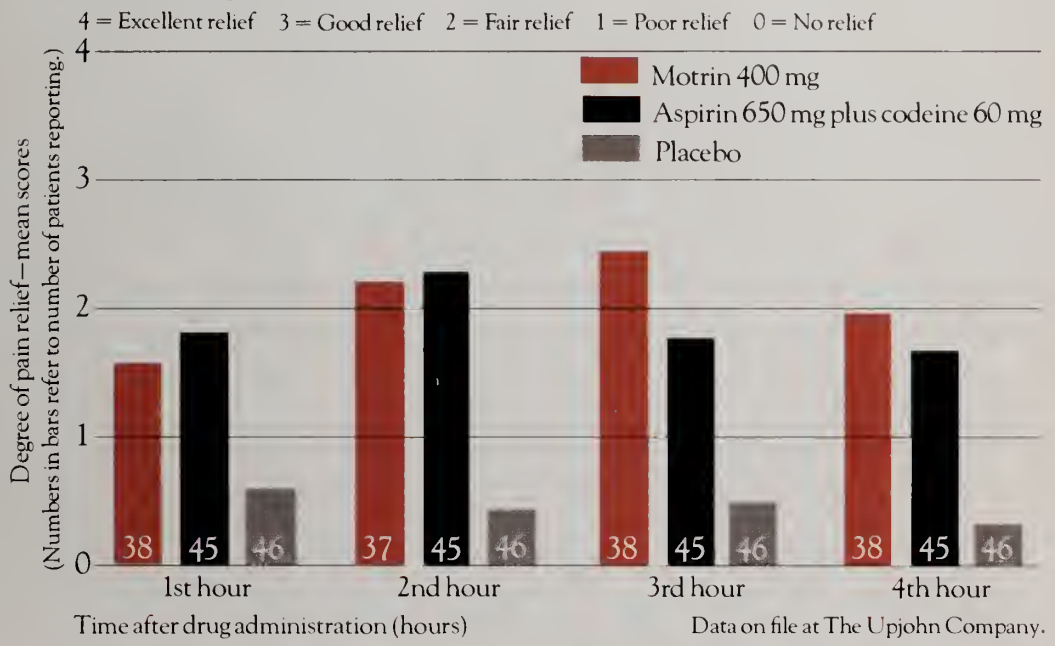

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Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

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*Incidence 3% to 9%.

Incidence less than 1 in 100

Gastrointestinal: Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

Causal relationship unknown

Gastrointestinal: Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

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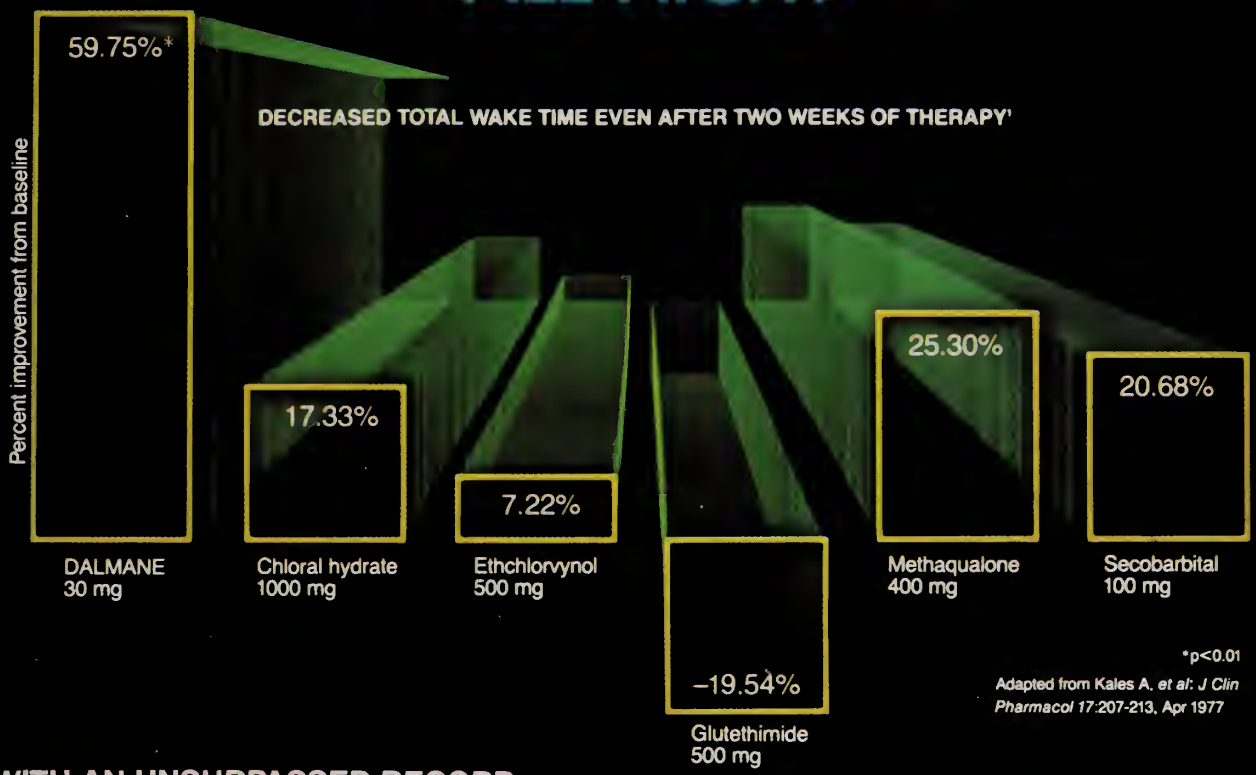

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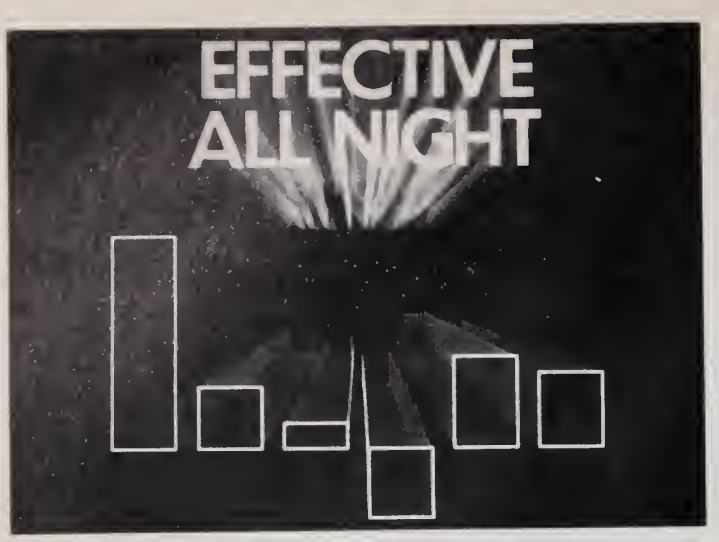

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–which can cause transient insomnia in the elderly[10]

–which can require careful monitoring in cardiovascular patients[10]

–which have strong anticholinergic effects[10]

Antihistamines

–which are *not* reliable sleep-inducing agents[11]

–which may produce stimulation instead[11]

–which have anticholinergic effects[11]

Major tranquilizers

–whose side effects may be troublesome for nonpsychotic patients[12]

–where tolerance for sedation appears rapidly[12]

Dalmane does not cause significant worsening of sleep beyond baseline levels upon discontinuation.[4]

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; in acute or chronic medical situations requiring restful sleep. Objective sleep laboratory data have shown effectiveness for at least 28 consecutive nights of administration. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended. Repeated therapy should only be undertaken with appropriate patient evaluation.

Contraindications: Known hypersensitivity to flurazepam HCl; pregnancy. Benzodiazepines may cause fetal damage when administered during pregnancy. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nighttime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, e.g., excitement, stimulation and hyperactivity.

Dosage: Individualize for maximum beneficial effect.
Adults: 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg recommended initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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Table IV (Cont.)

C. Central nervous system dysfunction

1. No focal findings suggesting space occupying lesion
   Immediate lumbar function
   Direct CSF examination by gram stain, acid-fast stain, India ink
   CSF culture for aerobes and anaerobes, mycobacteria, fungi; viruses if suspected clinically
   CSF serology: complement fixation for *coccidioides immitis;* antigen for *Cryptococcus neoformans*
2. Focal findings suggesting space occupying lesions
   Immediate CT scan or radioisotope scan
   (I) If positive - proceed to immediate neurosurgical consultation with open biospsy if
   not contraindicated. Specimens should be handled as in II.C. above.
   (II) If negative - consider EEG to R/O typical encephalographic changes of herpes encephalitis. Also consider detailed radiographic examination of entire neuraxis.

infiltrate is noninfectious.

The handling of specimens obtained by any of the procedurs should include immediate microscopic examination (including tissue silver strains for *Pneumocystis carinii* and fungi) and thorough culturing for routine and opportunistic pathogens (Table IV).

Antimicrobial Therapy

The initial choice of antibiotics is often empiric and must be made without waiting for results of cultures. Here it should be evident that a clear knowledge of the types of organisms that infect these patients becomes critical in the proper choice of antibiotics. In all specialty centers in which such patients are cared for, combinations of antibiotics are employed to provide broad coverage and in an attempt to obtain synergy against the offending pathogen. This usually includes a cephalosporin plus ticarcillin, carbenicillin, mezlocillin or piperacillin and an aminoglycoside.

With the advent of the third generation cephalosporins the therapy may change, but not until results of carefully performed studies are available to offer the physician guidelines for their use. If staphylococcal infection is suspected, the above regimen may be modified to include an aminoglycoside plus an antistaphylococcal antibiotic. If an antifungal agent is to be included in the regimen, amphotericin B is the durg of choice. Except in rare instances, miconazole and ketoconazole should not be used until the data on these durgs for disseminated infection can be carefully and critically evaluated by authorities in the field. This has not yet been done, yet these drugs are being used inappropriately in these patients. Empiric therapy must also be based upon continuing review of a hospital's predominant microbial isolates and their antibiotic sensitivities. Consideration of these factors should allow antibiotic choices to be made rationally rather than in a "shotgun" fashion.

Because these patients are at increased risk for the development of serious infections, empiric therapy should continue until granulocytopenia resolves, even if infection is not documented.

Antimicrobial Prophylaxis

Since the risk of nosocomial infection is high in these patients, especially during prolonged periods of severe granulocytopenia, attempts have been made to suppress normal resident microbial flora (gram-negative enteric bacilli, *S. aureus, C. albicans*) which cause most of these infections.

Protective isolation is not available in most hospitals and will not be discussed here. Because of this unavailability, recent regimens have been directed against protection of patients on open wards and private rooms. These have included skin disinfection with providone-iodine or chlorhexidine; nasopharyngeal sprays and mouth ointments containing either gentamicin, neomycin, polymixin B or amphotericin B or combinations of these, and oral administration of either trimethoprim-sulfamethoxazole alone or in combination with nalidixic acid, polymixin B or Amphotericin B to reduce gut flora without affecting colonization resistance. These regimens have been remarkably effective in reducing the incidence of major infections in ganulocytopenic patients and those undergoing induction chemotherapy. Further follow-up will be needed to determine the incidence of emergence of resistant organisms during and after such prophylactic measures since emergence of resistance already started.

In addition to it's use to rid the gut of aerobes, oral trimethoprim-sulfamethoxazole combination when used prophylactically has been shown to significantly reduce the risk of infection by *Pneumocystis carinii* in a variety of immunosuppressed patients. For discussion of the patient population in whom this may be effective, the reader is referred to the article by Hughes.

A. Is there a Role for Granulocyte Transfusions in Prophylaxis and Treatment of Infections?

This is perhaps the most controversial subject in relation to the management of the immunocompromised patient. To date it is generally agreed that prophylactic granulocyte transfusions should not be used, because they have not been demonstrated to significantly effect a reduction in the frequency of infections and in some instances have shown an increased risk of transfusion associated cytomegalovirus (CMV) infections. They also have caused sensitization of patients to platelets and leukocytes which have resulted in untoward reactions when patients have received platelet transfusions.

Results of investigations in which granulocytes have been given during periods of documented gram-negative bacterial or fungal infections together with antibiotics have not been

consistent. Some studies have shown a beneficial effect but only in those patients with prolonged granulocytopenia and microbiologically documented infection. In those patients in whom marrow recovery occurred during granulocyte therapy, the administration of granulocytes did not enhance recovery from the infections over that obtained with antibiotics alone. It should be appreciated that the use of granulocyte transfusions is not without undue hazards to both donor and recipient. An example of this in the recipient is the recent report that severe, sometimes lethal, pulmonary reactions, notably intra-alveolar hemorrhage, have ocurred in immunocompromised patients who were receiving amphotericin B concomitantly with granulocyte transfusions. The mechanisms are as yet unclear. If granulocyte transfusions are given to patients who also must receive amphotericin B concomitantly with granulocyte transfusions. at a different time than amphotericin B administration and in the setting of close pulmonary monitoring.

Prospects For the Future: Immunomodulators

The role of transfer factor (TF) in treatment of infections has never been satisfactorily defined. The first carefully performed study on its role as a preventive agent has recently been published: TF significantly reduced clinical chicken-pox during an outbreak of varicella in a cancer hospital. The effects of interferon (IF) have been notable in chronic hepatitis B infection, especially when given together with adenine arabinoside (ARA-A). The effect in other infections although present has not been remarkable, perhaps due to the lack of sufficient amounts of the agent, or purity, or both. This should be clarified with the purer preparations of IF now being produced. The role of other immunomodulators such as levamisole, thymosin, lithium, zinc and cimetidine has yet to be defined. Some of thse agents look very promising.

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QUIZ

Infections Complications In The Cancer Patients

1. The most frequent infection of patients with malignancies of the genitourinary tract is:

   a) Pneumonia
   b) Peritonitis
   c) Septicemia
   d) Prostatis
   e) meningitis

2. The percentage of infections is highest for patients with:

   a) Malignant lymphoma
   b) Hodgkin's disease
   c) Multiple myeloma
   d) Chronic lymphocytic leukemia
   e) Acute leukemia

3. Factors that increase susceptibility to infection, have analogs in tumors conditions, which of the following paired conditions is not true:

   a) Neutropenia - acute leukemia
   b) Lymphopenia - Hodgkin's disease
   c) GI ulceration - colonic carcinoma
   d) Impaired antibody production - Hodgkin's disease
   e) Local obstruction - bronchial carcinoma

4. The frequency of infection is related to the decrease in:

   a) Monocyte count
   b) Neutrophil count
   c) B-lymphocyte count
   d) Leukocyte count
   e) Red blood cell count

5. When patients with malignancies develop infections, the most frequent etiologic agents of fatal infections are:

   a) Bacteria
   b) Fungi
   c) Viral
   d) Protozoal
   e) Mycoplasmas

6. Fungal infections in cancer patients are more frequently seen in:

   a) Lymphoma
   b) Hodgkin's disease
   c) Acute leukemia
   d) Solid tumors
   e) Chronic leukemia

7. The most frequent bacterial pathogen in patients with acute leukemia is:

   a) Pseudomonas aeruginosa
   b) Escherichia coli
   c) Streptococcus pneumonia
   d) Hemophilus influenzae
   e) S. aureus

8. In the present decade in Cancer Treatment Centers the most feared pathogen is:

   a) Pseudomonas
   b) S. aureus
   c) Klebsiella
   d) Fungi
   e) Viruses

9. In Puerto Rico the most feared pathogen is:

   a) Pseudomonas
   b) S. aureus
   c) Klebsiella
   d) Fungi
   e) Viruses

10. The most frequent clinical presentation of an infection by Listeria monocytogenes in a cancer patient is:

    a) Pneumonia
    b) Meningitis
    c) Septicemia
    d) Disseminated
    e) Hepatitis

11. The fungal infections most frequently seen in a cancer patient are:

    a) Candida - histoplasmosis
    b) Candida - aspergillus
    c) Aspergillus - mucor
    d) Histoplasmosis - cryptococcosis
    e) Cryptococcosis - aspergillus

12. Diffuse lung infiltrates and severe hypoxemia in an immunocompromised host, suggest:

    a0 Histoplasmosis
    b) Pneumocystis carinii
    c) Strongyloidiasis
    d) Legionella
    e) Pneumococcal disease

(See answers on page 48)

PRESENTACION DE CASOS

FIRST CASES OF BOTULINIC PARALYSIS IN PUERTO RICO

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Abstract: In August, 1978, three cases of botulism (one fatal) associated with ingestion of marinated fish occured in Puerto Rico. This is the first known outbreak of botulism on the island. The fish preparation, known as "sierra en escabeche" is locally quite popular, and its high vinegar content should make the growth of *Clostridium botulinum* unlikely. Type A botulinal toxin was identified in the suspected foood product and in the serum of two of the three patients; pH of the fluid phase of the food was under 4.6.

Botulism is rarely reported from the Caribbean, and had not been reported from Puerto Rico until now. Since it is generally accepted that *Clostridium botulinum* does not grow in acid medium (pH 4.6 or less),[1] a product marinated in vinegar would not be suspected as the source of an outbreak. For these reasons, we are reporting an outbreak of foodbourne botulism in Puerto Rico, in which marinated kingfish ("sierra en escabeche") was the vehicle. The investigation was made possible by the prompt notification to the Puerto Rico Health Department of the suspected diagnosis in the index case and resulted in the location, treatment, and eventual recovery of a patient who, if undiagnosed and untreated, would probably have died.

Case Reports

Patient 1, a 46-year-old Guaynabo resident, was admitted to the emergency room of a hospital at 1:00 A.M., August 10, 1978, with vomiting, weakness, ptosis, and blurred vision. No sensory abnormalities were noted. He reported having had an apparent allergic reaction to fish 2 years before, which consisted of facial swelling and a rash, and he blamed his current symptoms on fish he had eaten the previous day at noon. As dysphagia and recumbent dyspnea developed, a neurologist was consulted and made the clinical diagnosis of botulism.

The physical examination on admission revealed an alert, distressed patient with bilateral ptosis and ophthalmoplegia; sluggish pupillary, corneal, and gag responses; dry mouth; dysphonia; dysarthria; and inability to extrude the tongue. Muscle tone was generally decreased, particularly at the neck and shoulders, with marked kyphotic posture and shallow, labored respirations when sitting. There were no apparent cerebellar, sensory, language, or peripheral reflex deficits. The patient was electively intubated and, within 24 hours after diagnosis, received, about 9 hours apart, two doses (each consisting of one vial IV and one vial intramuscularly) of trivalent botulinal anti-toxin (Connaught Laboratories; 7,500 units of type A, 5,500 units of type B, and 8,500 units of type E antitoxin per vial) without noticeable improvement. Lumbar puncture and edrophonium test results were negative. His course was complicated by fever (38.8°C), hypertension (maximum 180/130), paralytic ileus, oliguria, tachycardia, and hypotension. He died August 12. No autopsy was performed.

Patient 2, a 24-year-old employee of Patient 1, was hospitalized on August 8, after 4 days of weakness, blurred vision, a sensation of pressure in the neck, and complaints of drowsiness, lightheadedness, and headache. On examination he had mild bilateral ptosis, dysphagia, and shoulder and neck weakness. By August 10, 1978, when the diagnosis of botulism was made, he was slightly improved and was not given antitoxin. he was discharged on August 17, still feeling some weakness.

Patient 3, a 16-year-old employee of Patient 1, was found by author (VV) prostrate at home in a remote rural community on the afternoon of August 10, 1978. He had complained of headache the previous evening and had awakened that morning with abdominal pain, vomiting, dizziness, headache, somnolence, severe weakness, and dysarthria. he was admitted to an ICU in mildly distressed condition, with obvious lethargy, well oriented and forcefully resisting examination. Pertinent physical findings included mild bilateral ptosis, horizontal nystagmus to the right —a familial condition— but otherwise normal extraocular movements, adequate pupillary and corneal reflexes, poor gag response, and difficulty with tongue motion. Weakness of large muscles was initially minimal, and rectal sphincter tone was normal. There were no apparent cerebellar, sensory, language, or peripheral reflex deficits. Respiratory muscles became progressively weaker through the night, and he was intubated and given ventilatory assistance. Within 24 hours of admission he received two doses (each consisting of one vial IV and one vial IM) of trivalent (ABE) botulinal

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antitoxin. Episodes of sudden flushing, sweating, anxiety with tachycardia (up to 125), hypertension (up to 150/100), and hypotension were documented over the next 2 days. Cranial nerve deficits and muscle weakness (anisocoria, ptosis, ophthalmoplegia, masseter and sternomastoid paralysis, and weakness of all extremities) were maximal from August 14 to 20 but returned to normal by September 7. He was discharged November 7, still weak, but walking without assistance.

Epidemiologic Investigation

On August 10, 1978, information was obtained form the reporting neurologist, Patient 1, and the patient's wife. Concern quickly focused on a homemade marinated kingfish ("sierra en escabeche") the patient had eaten the day before. It was then realized that Patient 2, who had already been sick for a few days, and Patient 3, absent from work that day, had also eaten the marinated kingfish. The suspected foood was confiscated, and other persons who might have been exposed were traced and alerted. Patient 2 and his physicians were informed of the situation and, at the same time, Patient 3 was found at home and referred for appropriate care. The Food and Drug Administration (U.S. Department of Health, Education and Welfare) and the Food Hygiene Division (Puerto Rico Department of Health) were notified. Trivalent (ABE) botulinal antitoxin, requested by telephone from the Center for Disease Control (CDC), was received 12 hours after request, and was administered to Patients 1 and 3 but not to Patient 2, who was showing signs of recovery. The antitoxin was given before results of toxicity tests on the patients' sera were known.

The wife of Patient 1 had prepared the kingfish on July 22, using the customary method (frying the slices of fish and then marinating them in a mixture of oil, vinegar, onions, peppercorns, and bay leaves). She stored the fish in three large glass jars, closed with screw caps (the fish is usually placed in wide open trays) and left it to "cure" under a table in her husband's cafeteria-pizzeria business. It was prepared for home consumption and never sold to the public (mostly students from the school next door). Patient 1 and his wife ate some fish the next week and gave some to neighbors, who ate it the same day. Patient 2 ate some of the fish on August 2, 3, and 4 and began feeling ill on August 5. Patient 3 ate small amounts of fish on August 8 and 9, and began to feel ill on August 9. Patient 1 again ate some fish at lunch on August 9 and may have done so the day before. The father and two other employees of Patient 1 tasted the fish between August 4 and 9 but did not become ill. Everyone remembered that the fish tasted good.

Laboratory Results

Type A botulinal toxin was identified (by the Anaerobe Laboratory, CDC, with a mouse neutralization test[2] in serum samples obtained August 10 from Patients 1 and 3 but not in the serum of Patient 2. A second serum sample was obtained from each patient on August 11, several hours after Patients 1 and 3 were given antitoxin. No toxin was detected in any of these specimens. A stool specimen was obtained on August 11 form patient 2; no botulinal toxin was detected, and no *C. botulinum* was isolated.

The contents of the three jars of marinated fish were also examined in the laboratory (Table). The amount of fish and liquid remaining in each jar was different (since the first jar was quite full, none of its contents may have been consumed). Type A botulinal toxin was detected in samples from all three jars. *C. botulinum* was isolated from enrichment cultures of fish from jars 2 and 3; it was detected with mouse toxicity tests in the enrichment culture of the fish from jar 1, but the organism was not isolated.

TABLE

Laboratory Findings for Three Jars of Marinated Fish

Jar Number	Fullness of Jar*	Toxin Assay** (Mouse lethal dose/gram fish) Minimum	Maximum	pH+
1	8 inches	4	20	4.5
2	5.5 inches	4,000	20,000	4.4
3	3 inches	4	20	3.9

* Each jar was 10 inches tall; the fullness was the outside measurement of the height of the contents remaining.
** Type A botulinal toxin, detected in mouse assay of extract of a 75 gram piece of fish.
\+ The pH was measured on a sample of fluid from near the bottom of the jar.

Discussion

The symptoms of botulism may suggest a large number of infectious, pharmacologic, or neurologic syndromes[2]. Of particular concern in this incident was the possibility that the outbreak involved "ciguatera" poisoning, a fish-associated intoxication occasionally seen in Puerto Rico, which can produce cranial nerve palsies and respiratory paralysis when very severe.[3] Ciguatera is usally associated with marked sensory disturbances, which none of the three patients had, so botulism continued to be the working diagnosis while confirmatory tests were performed.

The heat-resistant spores of *C. botulinum* are found through out terrestrial and marine environments and can therefore be present in many kinds of vegetable or animal products. Surveys of marine specimens from the U.S. Gulf coast and the coasts of Venezuela, Brazil, and Central America have shown the presence of *C. botulinum* types A through F. Type E predominates along the U.S coast, whereas types A and C are more common near Venezuela.[4] No surveys for the organism have been done nearer Puerto Rico.

Prompt investigation of this incident after diagnosis of the first case resulted in immediate identification and location of the two additional cases and confiscation of the contaminated food item. Since the "escabeche" was not prepared in the vegetable-home-canning manner that is often associated with outbreaks of botulism, we wished to determine what conditions had allowed the germination of the organism in the marinade. There was air in the jars, but the thick layer of oil between air and solution created a

virtually anaerobic environment. The measured pH in all three jars was 4.5 or lower, a level at which there is little risk of botulism.[1,5] The vinegar may not have completely or quickly penetrated the fish, leaving the interior pH sufficiently high for local spore germination, vegetative growth and toxin production. We could not test this hypothesis because the long period of soaking of the fish in the vinegar (19 days at the time of recognition of the cases) and the shaking of the jar contents on shipment to the Laboratory would no doubt have insured equilibration of the pH throughout the entire product. In addition, a recent report[6] shows evidence that *C. botulinum*, in the presence of other microorganisms and protein-rich substrates, can grow and produce toxin at pH levels as low as 4.0.

None of the four people who ate of the fish in the last week of July became ill at that time, but three of six who ate in early August developed botulism. Some individuals who consume incriminated items do not become ill, perhaps because the toxin is not evenly distributed throughout the food.[7] Although as little as 1 microgram of toxin (about 200,000 mouse intraperitoneal lethal doses) may be lethal for a human being,[8] It is quite possible that a human could ingest 100-200 mouse intraperitoneal lethal doses with impunity (about 25 grams of fish from jars 1 or 3, in this case, (Table). The people who became ill may have eaten only from jar 2, in which the fish had a thousand-fold greater toxin concentration than in the other two containers. The incubation period for these cases of botulism was well within the recognized limits (a few hours to 8 days)[2] but it could be as short as 12 hours for Patient 1 or as long as 72 hours for patient 2. Although recovery from botulism can be protracted, the prolonged respiratory insufficiency in Patient 3 was complicated by nosocomial infections and eventually by severe muscle wasting.

Afther they were given antitoxin, Patients 1 and 3 did not have detectable levels of toxin in serum. This is as expected, since the antitoxin dose provides far more than enough antibodies to neutralize circulating toxin. A large portion of therapeutic botulinal antitoxin given IV is detectable in the circulation within 1 day after it is given, and, in a limited number of observations, a half-life of 6-7 days has been calculated (CDC Anaerobe Laboratory, unpublished data). Antitoxin was not given to Patient 2 because in his stable, mildly ill condition, the risk of side effects from antitoxin (a horse serum preparation) outweighed its possible beneficial effects. The reaction rate can be near 10%,[9] whereas the level of efficacy of botulinal antitoxin is in question.[10]

On a review of the records of the Communicable Diseases Control Program of the Puerto Rico Department of Health and with the considerable publicity given to this outbreak by the news media, no reports of botulism, confirmed or suspected, or of illnesses that could be diagnosed retrospectively as botulism, came to light. Also, the source of this outbreak was an acid food with a pH considered unsatisfactory for growth of *C. botulinum*. Therefore, this incident was not representative of a widespread public health problem but was a unique event in the Island.

Resumen: **En agosto de 1978 tres casos de botulismo (uno con desenlace fatal), asociados a la ingestión de pescado en escabeche, ocurrieron en Puerto Rico. Este es el primer brote conocido de botulismo en la isla. El alimento implicado, sierra en escabeche, se consume frecuentemente en Puerto Rico y su alto contenido de vinagre debería imposibilitar el crecimiento de *Clostridium botulinum*. Se identificó toxina botulínica tipo A en la comida sospechosa y en el suero de dos de los tres pacientes. El pH de la fase líquida del alimento era menor de 4.6.**

Acknowlegmentes

Recognition is due to Dr. Norberto J. Arbona, Neurology Institute, Hospital Metropolitano, Río Piedras, Puerto Rico, who notified the Puerto Rico Department of Health of the suspected diagnosis of botulism for the index patient, and Mrs. Loretta M. McCrosky, Anaerobe Laboratory, Centers for Disease Control, for her excellent laboratory assistance.

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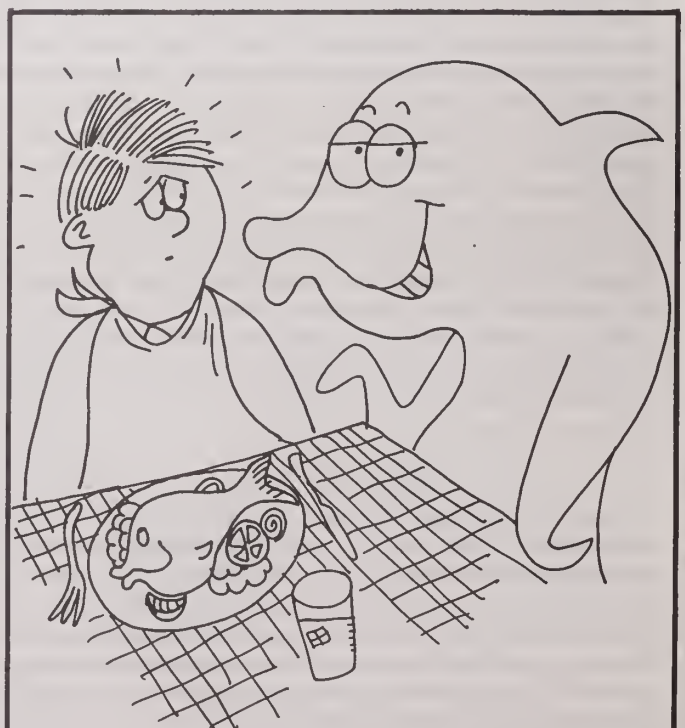
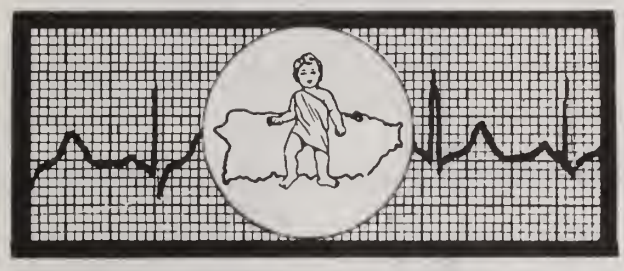


Enjoy your dinner, remember "Ciguatera"

Sección de AutoEVALUACION

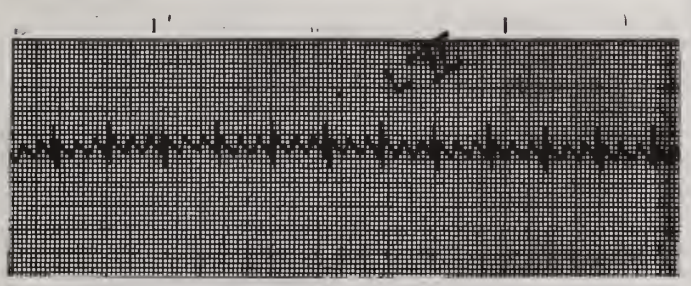


CASOS DE ELECTROCARDIOGRAFIA PEDIATRICA

Rafael Villavicencio, MD

GGM es un infante de 6 meses de edad que es llevado al Pediatra por fiebre, tos y dificultad respiratoria de 24 horas de duración. Al examen se aprecia un niño acianótico, con una temperatura rectal de 39°, frecuencia respiratoria de 80/minuto, retracciones subcostales, y una frecuencia cardíaca rápida. Los sonidos cardíacos eran buenos y no se apreciaba soplo significativo.

Fue referido para evaluación cardiovascular y se obtuvo el siguiente trazado:



El diagnóstico electrocardiográfico correcto es:
a) taquicardia supraventricular
b) aleteo ("flutter") atrial
c) trigeminismo atrial
d) fibrilación atrial
e) bloqueo A-V 2:1

Repuesta: b) Aleteo ("flutter") atrial

Definición: El "flutter" atrial (FA) es una taquidisritmia que se caracteriza por la presencia de ondas P regulares, de apariencia ondulada y a una frecuencia entre 250 y 450/minuto. Se le denomina "flutter" o aleteo por la semejanza entre la apariencia festoneada de las ondas P y el movimiento de las alas de las aves.

Criterios Diagnósticos

1. Los intervalos R-R son regulares
2. Tiene complejos QRS rápidos
3. La apariencia festoneada o cerrada ("sawtooth" de las ondas P es la característica electrocardiográfica principal del FA. A este tipo de ondas se les llama ondas F.
4. La frecuencia auricular oscila entre 250 y 450/minuto. Esta va a depender de: la velocidad de conducciõn, del período refractario del nodo AV, y de la respuesta autonómica.
5. La transmisión de los impulsos atriales a los ventriculos puede ser en el orden de 1:1 2:1, ó 3:1. El tipo de conducción más frecuente en niños con FA es de 2:1.

Análisis del Trazado

En el caso que se presenta pueden apreciarse los intervalos R-R regulares, y una frecuencia ventricular de 140/minuto con complejos QRS normales.

Es obvia la presencia de ondas F peristentemente regulares y de apariencia serrada a una frecuencia de 420/minuto. Este FA tiene una respuesta ventricular de 3:1.

Mecanismos

Se han propuesto varios mecanismos[1] para explicar la aparición del FA.

1. *Mecanismo de reentrada* - atribuye el FA a un impulso que establece un circuito en el músculo atrial y conduce a través de este circuito de una forma repetitiva.
2. *Automatismo* - los que lo apoyan proponen que el FA es causado por la descarga de un foco automático ectópico.
3. *Disritmia* - Por ese mecanismo algunos estímulos prematuros pueden provocar descargas atriales rápidas ocasionando el aleteo auricular.

Recientes estudios electrofiosológicos invasivos en niños han demostrado que el FA puede inducirse fácilmente por medio de la estimulación eléctrica programada, lo que favorece un mecanismo por reentrada.[2]

Situaciones Clínicas

El FA es poco frecuente en la edad pediátrica y no suele estar asociado a cardiopatias congénitas en la mayoría de los casos. Puede presentarse *in utero*, manifestándose por latidos fetales irregulares.

Aunque usualmente ocurre espontáneamente, hay ocasiones, como en el caso presentado, en que está precedido de una enfermedad febril. Cuando el FA aparece pasada la infancia suele ser asociado a defectos cardíacos en donde hay atrios grandes e irritables.

Puede aparecer luego de cirugía atrial, en desbalance electrolítico severo, hipoxia, e hipoglucemia.

Tratamiento

Debe ser de instauración inmediata, pues el FA conduce a fallo cardíaco rápidamente.

1. *Maniobras vagotónicas*- no se rcomiendan en FA ya que son inefectivas y potencialmente peligrosas.
2. *Digoxin* - por vía endovenosa en las dosis usualmente recomendadas de acuerdo a la edad y peso del paciente. Por su efecto directo sobre las células del músculo atrial se disminuye la velocidad de conducción y se aumenta el período refractario, interrumpiendo de esta forma el circuito de reentrada o disminuyendo la respuesta atrial a un posible foco automático.
   Si el digoxin solo no es efectivo en convertir el paciente a ritmo sinusal se añaden otros medicamentos como *quinidina* o *propranolol.*
   Se debe tener mucha precaución al utilizar conjuntamente quinidina y digoxin ya que su combinación puede elevar la concentración sérica de digoxin a niveles tóxicos.[3]
3. *Cardioversión eléctrica* - es el método de elección para la conversión de un paciente hemodinámicamente afectado con FA. Es casi siempre efectiva, aún utilizando dosis bajas de energía. (0.5 Watt-sec/Kg)

Pronóstico

En la mayoría de las series significativas de FA en niños se reporta una alta incidencia de efectividad en su conversión a ritmo sinusal con digoxin o en combinación con quinidina y/o propranolol.

En cambio, en infantes con FA y anomalias estructurales cardíacas el pronóstico no es bueno.

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ELECTROCARDIOGRAM OF THE MONTH

Charles D. Johnson, MD

Giant Massive T Wave Inversions With Prolonged Q-T Intervals

This 58-year old woman presented peculiar "spells". her electrocardiogram (ECG), Figure 1, demonstrated complete atrioventricular (AV) block; giant massive T wave inversions with prolonged Q-T intervals.

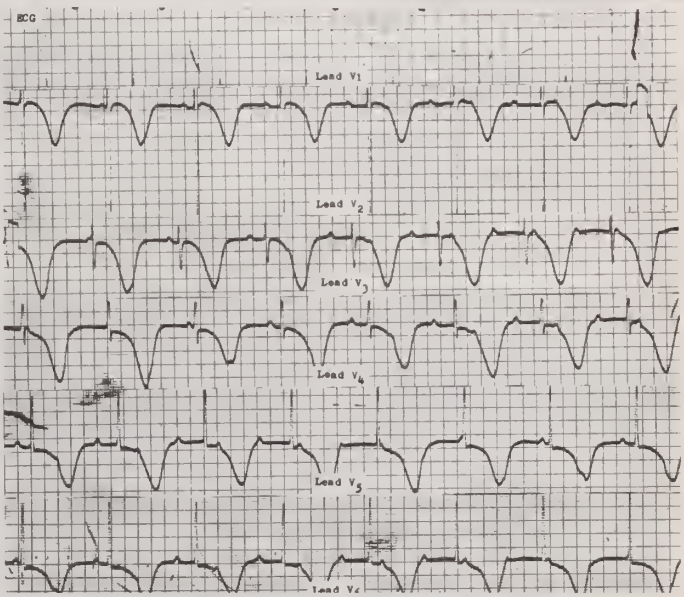

Figure 1. P rate = 100 per minute (P-P interval = 600 msec.). No positive ventriculophasic phenomenon (Erlanger-Blackman).
P waves peaked in leads II, III, aVF, V_{4-6}.
QRS rate = 46 (R-R = 1300 msec.).
QRS width = 0.08 sec., essentially regular, idiojunctional, Axis O°.
Left ventricular hypertrophy.
Q-T interval = 800 msec., Q-TC = 0.70 sec. = 179 percent (165 percent).
Giant T wave inversions in leads I, II, aVL. Maximal T depth 21 mm; maximal T width 0.52 sec.

Discussion

Giant Massive T Wave Inversions with Prolonged Q-T Intervals involve a number of conditions and differential diagnoses:

1. Stokes-Adams attacks of syncope, and even cardiac arrest and convulsions, associated with complete, advanced and 2:1 second degree AV block - the "das post-synkopale Bradycardie-Stoffwechsel Syndrome" of Holtzmann. Such electrocardiographic changes are almost pathogomonic of a recent syncopal Stokes-Adams attack with loss of consciousness due particularly to ventricular fibrillation, or to standstill or multiform ventricular flutter, i.e., torsade de pointes.

   The T waves are bizarre, distorted, asymmetrical, broad and deep. Their duration may vary from 260-640 msec. and the depth from 0.5 -3.2 mv (32 mm). The changes are best seen in leads $V_{2\ 4}$. The T waves can be upright (13-15 mm in lead III. The Q-T intervals are markedly prolonged - 0.56 - 1.04 sec. The Q-TC interval may be increased to 200 percent (normal 0.39 - 425 sec.).

   The changes may be unstable but often persist for hours or days. The escape rhythm may be either idiojunctional or idioventricular. A long Q-T interval has rarely been associated with congenital complete heart block, with second degree AV block and with sinus bradycardia and AV dissociation.

2. Bradycardias - secondary to sinoatrial node disease (severe sinus bradycardia) or AV block associated with Stokes-Adams attacks. The slow ventricular rates may range from 34-50 per minute. T wave inversions correlate with the duration of R-R intervals.

Pathogenesis for Numbers 1 and 2.

   a. Intense sympathetic stimulation resulting from the hypoxia of a syncopal attack.
   b. Variable vagal tone. Cerebral reflexes.
   c. Long duration of diastole in bradycardia. The increased intraventricular volume (distention) and pressure may delay repolarization of a locally damaged heart. Response of the ischemic myocardium. Difference in metabolic response.

3. Ischemic Heart Disease - Prinzmetal Variant Angina
   Acute anterior epicardial ischemia (coronary insufficiency)
   Transmural myocardial infarction (MI)
   Subendocardial MI
   Sudden Death after MI

The T waves are norrow, sharp, symmetrical and deeply inverted, up to 29 mm. They may revert in 1-20 days. Large U waves.

4. Cerebral Disorders - Subarachnoid hemorrhage, noteworthily, (specially anterior fossa) "CVA's".
   Rupture of aneurysm. Infarction, Embolism.
   Tumors. (primary and metastasis) Head injuries. Skull fracture. Hypertensive encephalopathy.
   Neurosurgical procedures - angiography, pneumoencephalography. Cryohypophysectomy.
   Experimentally-induced. Stimulation of left stellate ganglion and section of the right.
   Psychologic stress, syncope, ventricular ectopy and fibrillation. Transient injury or ischemia of cerebral autonomic centers.

   Prolonged Q-T interval and the T waves may be huge and inverted or upright. U waves large.

5. Right Ventricular Enlargement and Strain.
6. Metabolic Disturbances:

   a. Hypokalemia - T and U wave fusion.
   b. Hypomagnesemia. Increased Na.
   c. Hypocalcemia. Malabsorption (cerebral & ionic changes). Kwashiorkor.
   d. Beriberi heart disease.
   e. Hypothyroidism.
   f. Corticosteroids in congenital or acquired (MI) complete AV block; reversible; may be due to low potassium, stretching of myocardium from diastolic overload; local ionic distribution; perversion of myocardial repolarization.

   T Wave Inversions on Unpaced Postpaced ECG's:

   Profound T inversions and ST segment depression.
   Right ventricular endocardial and left ventricular epicardial pacemakers.

   These occur mainly in the first postoperative week, but can occur as early as the first 24 hours or as late as 4 weeks after pacing. They may disappear but this may require months or 1-2 years, depending upon the duration of pacing (10 minutes- 4 3/4 years). Due to ventricular depolarization from an abnormal site. Can be seen also with sinus or junctional rhythm, and left or right bundle branch block.

8. Asymmetrical Pacemaker Spike on T wave summit. (R-on-T). Very rare.
9. Coronary Arteriography - Deepening and expansion of T waves. Natural coronary arteries, bypass grafts, internal mammary artery implants.
10. Congenital Hereditary Prolonged Repolarization Syndromes
    Jervell and Lange-Nielsen syndrome - cardioauditory.
    Romano-Ward syndrome. (Hereditary imbalance of right & left sympathetic innervation of heart under emotional, physical or auditory stres).
11. Torsade de Pointes - virtually always associated with prolonged Q-T interval. Many associations and causes, as listed.
    Asynchronous or heterogenous repolarization, or temporal dispersion of repolarization, or temporal dispersion of repolarization of the left ventricle. Asymmetrical ventricular activation. Reentry.
12. Drugs:
    Class 1 antiarrythmic drugs: a. Quinidine syncope, b. Procainamide, IV in a case of preexcitation induced transient bradycardia, 2:1 and complete AV block, slow idioventricular rhythm and massive negative T waves. c. Disopyramide.
    Amiodarone. Digitalis + auxamethonium.
    Psychopharmacologic drugs - Phenothiazines - thioridazine, perphenazine. Tricyclic antidepressants-amitryptiline.
    Diuretics. Coronary vasodilators (phenylamine, lidoflazin). Certain experimental drugs.
13. Mitral valve prolapse.
14 Miscellaneous:
    The T waves may be deeply inverted in the precordial leads. Hypertensive Heart Disease with congestive heart failure. Aortic stenosis. Left strain variant. Mitral stenosis. AV Canal Defect, Chronic cor pulmonale. Chronic constrictive pericarditis. Myocarditis. Myotonic Dystrophy. Diphtheria. Hypothermia. Influenza. Right bundle branch block. Alcohol ingestion. Acute abdomen. Liquid protein diets (rapid weight loss). Sudden Infant Death Syndrome (Sleep Apnea). Valsalva Maneuver. Exercise. Acute pneumothorax. Increased sympathetic discharge. Cardiac depressants-IV mercurials. Arsenic. Combinations. No cardiac disease.

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Abstractos de La Literatura Médica

TRATAMIENTO QUIRURGICO DEL DUCTO ARTERIOSO PATENTE EN INFANTES PRE-TERMINO: Eggert LD, Jung AJ, McGough EC, Ruttenberg HD. Ped Cardiol 1982, 2:15.

Se informa la experiencia en 79 neonatos pre-término con síndrome de membrana hialina a los cuales se les ligó un conducto arterioso persistente en la unidad de cuidado intensivo neonatal. Las indicaciones para cirugía fueron: 1) corto-circuito de izquierda a derecha grande por aortograma o agrandamiento del atrio izquierdo por ecocardiograma con uno o más de los siguientes: 2) retención de CO_2 y dependencia de respirador, 3) fallo cardíaco congestivo refractario al tratamiento, 4) incapacidad para ganar peso.

La mortalidad en el primer mes fue de solo un 9% y fueron debidas a complicaciones médicas pre-existentes. La morbilidad fue rara.

Concluyen los autores que el cierre quirúrgico del ducto arterioso persistente en infantes pre-término puede ser un procedimiento seguro y eficaz cuando el cierre farmacológico del mismo es inefectivo o está contraindicado. Más aún se demuestra que este procedimiento puede realizarse en la unidad de cuidado intensivo neonatal sin necesidad de transportar a un quirófano a estos infantes en estado crítico.

Rafael Villavicencio, MD

CLINICAL FEATURES OF SYSTEMIC LUPUS ERYTHEMATOSUS: DIFFERENCE RELATED TO RACE AND AGE OF ONSET: Balloy SP, Khan MA, Kushner I. Arthritis and Rheum. 1982, 25(1).

The frequency of clinical features of systemic lupus erythematosus (SLE) and determined survival in 113 patients with younger-onset lupus (age below 55 at clinical diagnosis) and 25 patients with older-onset lupus (age below 55 at diagnosis) was compared. The most striking difference was in the racial distribution; 59% of the younger patients were black, compared with only 20% of the older-onset patients (P 0.001). Major manifestations of lupus, including clinically evident renal disease, central nervous system involvement, and cutaneous involvement, occured with similar frequency in both age groups. Antibodies to DNA were detectable equally often in both groups, but hypocomplementemia was more common in the younger patients. Five-year survival in the younger-onset group (79%) was similar to that of the older-onset group (72%); there was a tendency toward relatively improved survival in patients in the latter group when compared with the expected survival of appropriately matched control populations. Major significant differences in racial distribution included 1) a higher incidence of serositis in older whites and in blacks regardless of age, and 2) more frequent hypocomplementemia in younger patients within both racial groups.

Edwin Mejías, MD

PREDICTIVE VALUE OF RADIONUCLIDE JOINT SCINTIGRAMS: Shearman J, Daile D, Hawkins D, Rosenthal L. Arthritis and Rheum. 1982, 25(1).

Twenty-two patients with normal or "noninflammatory" 99m technetium-labeled polyphosphate (TPP) peripheral joint scintigrams taken between 1974 and 1976 were reevaluated clinically. Retrospective chart review revealed that all initially had persistent polyarthralgia of more than 3 months duration. At followup, a mean of 3.6 years later, none had evidence of inflammatory joint disease, although 1 patient had systemic lupus erythematosus and 2 had polymyalgia rheumatica. A noninflammatory joint scintigram as as part of a thorough rheumatologic evaluation may be a useful procedure in excluding inflammatory joint disease in selected patients with chronic persistent polyarthralgia.

Edwin Mejías, MD

STAPHYLOCOCCUS EPIDERMIDIS - NO SERA DESCONTINUADO: Christensen GD, et al. Ann Int. Med. 1982, 96:1

Staphylococcus epidermidis ha sido considerada como una bacteria no patógena excepto en casos de heridas, cuando se usan prótesis, o se utilizan "shunts" cerebroespinales. *S. epidermidis* ha sido aceptado como el causante de la endocarditis en pacientes con enfermedades o reemplazos en las válvulas cardiacas. Ha sido aislado de catéteres intravasculares, pero usualmente descartado como un contaminante o colonizador no patogénico.

Christensen y asociados hicieron una revisión de 26 casos de septicemia. 11 casos indicaban claramente la presencia de *S. epidermidis;* 16 casos sólo sugirieron sepsis por este organismo. Ellos caracterizaron los pacientes clínica y

microbiológicamente y analizaron los factores epidemiológicos que podrían estar contribuyendo.

Los 11 pacientes con sepsis por *S. epidermidis* tenían, por lo menos, un cateter intravascular principal en el lugar colonizado por el organismo; el 59% de los cultivos de sangre resultaron positivos para *S. epidermidis;* ésto fue demostrado en más de uno de los cultivos utilizando biotipo con fago o antibioculares que permanecieron en el interior por largos períodos de tiempo y los que se utilizaron para hiperalimentación. Dos de los once pacientes, que presentaron fiebre de una o más semanas de duración, eventualmente murieron de sepsis.

Los 16 pacientes en que se sospechaba sepsis por *S. epidermidis* presentaron cuadros clínicos menos severos, con fiebres bajas y de menor duración. Estos pacientes también estaban con tratamiento endovenoso. Hubo crecimiento de *S. epidermidis* en solo 50% de los catéteres, y solo 20% de los cultivos de sangre resultaron positivos. Dos pacientes de este grupo aparentemente murieron de sepsis. Se hicieron autopsias en 3 de los 4 casos de muerte y se demostró la formación de abscesos y pulmonía por *S. epidermidis.*

Epidemiológicamente, se asociaron los casos con la higiene en las técnicas médicas y de enfermeras y con el cuidado de los catéteres. Cultivos de las manos y nariz demostraron una alta razón de portadores de *S. epidermidis* en un número significativo del personal. Los microorganismos que se aislaron de la sangre de pacientes y de catéteres eran, en su mayoría, resistentes a antibióticos, a diferencia de los que se aislaron de áreas de la piel escogidas al azar. Estos microorganismos resistentes eran del mismo tipo de los que se aislaron de los médicos y enfermeras. Comparando con *S. epidermidis* aislados de cultivos de peil, más de la mitad de los aislados sépticos eran resistentes. Los patrones de resistencia a antibióticos eran extremadamente variables, pero la resistencia a clindamicina, tetraciclina, cloramfenicol, penicilina y ampicilina era frecuente.

C.H. Ramírez-Ronda, MD

DUODENAL ULCER DISEASE IN THE HOSPITALIZED ELDERLY PATIENT: R.P. Permutt and J.P. Cello. Digestive Diseases and Sciences 1982, 27:1.

Los autores evaluaron los records médicos de todos los pacientes admitidos al Hospital General de San Francisco entre julio del 1977 a mayo del 1980 en quienes se documentó una úlcera duodenal por endoscopía o cirugía. Cuando separaron a los pacientes en dos grupos, menores de 60 años y pacientes de 60 años o más, encontraron algunas diferencias significativas entre los grupos. El grupo de mayor edad, por ejemplo, tuvo una frecuencia mayor de recurrencia de sangramiento en el hospital, se transfundió más, tuvo una hospitalización más prolongada y una mortalidad mayor (15% vs. 2%).

Angel Olazábal, MD

A CONTROLLED CLINICAL TRIAL OF THE EFFICACY OF THE HEPATITIS B VACCINE (HEPATITIS B): A FINAL REPORT: Szmuness W., Stevens CE., Zany EA., et al, Hepatology 1981, 1:377-85

Se evaluó la efectividad de una vacuna en contra de hepatitis tipo B en una población de hombres homosexuales (que tienen un riesgo aumentado de adquirir la enfermedad). La vacuna se preparó de partículas de antígeno de superficie (HBsAg) inactivadas en formalina. Se incluyeron en el estudio 1083 hombres y el tiempo de seguimiento fue de 24 meses. Más de un 95% de los vacunados desarrollaron el anticuerpo contra el antígeno de superficie. 3.2% de los vacunados desarrollaron hepatitis tipo B versus 25.6% de los que recibieron la vacuna placebo ($p < 0.0001$). No hubo diferencia significativa en la incidencia de efectos nocivos secundarios entre el grupo que recibió la vacuna y el grupo placebo.

Angel Olazábal, MD

CORRIENTE GALVANICA, SU USO EN LA CONSOLIDACION DE FRACTURAS: Muñiz de Carvalho A, T. Bueno O J, Ferreira López, S.M. Revista Da Associacao Médica Brasileira. Vol. 26 - No. 7 pp 226-228 1980.

Estos autores demostraron el estímulo de osteogénesis en la consolidación de fractura a través de una corriente directa (galvánica), como medio de tratamiento secundario conservador de fracturas con seudoartrosis o retardo de consolidación. Los resultados fueron plenamente satisfactorios, principalmente para casos de seudoartrosis normales, o sea, sin infección. En algunos casos de fractura reciente, en pacientes entre 10 y 48 años con fracturas diafisarias de radio, ulna y clavícula, respectivamente, presentaron resultados muy buenos por el tiempo transcurrido y por la firmeza del callo producido.

Gilda Davis, MD

INTRAARTICULAR STEROIDS IN THE TREATMENT OF ROTATOR CUFF TEAR: Weiss, J.J.: Arch. Phys. Med. Rehab. 62:555, 1981.

En estudios previos se ha dudado de la eficacia de la inyecciónde esteroides al espacio intraarticular en el tratamiento de rupturas parciales del manguito del rotador. En este estudio se utilizó artrografía para corroborar el diagnóstico y para hacer la inyección de esteroides. Se obtuvieron resultados exitosos en 13 de 15 pacientes. Se aduce que la inyección intraarticular de esteroides es un tratamiento adecuado para roturas parciales del manguito del rotador.

Frank W. López, MD

INEFFECTIVENESS OF LEVAMISOLE IN SYSTEMIC LUPUS ERYTHEMATOSUS: Ta Hsin Ha, Decker, JL et al: Arthritis and Rheumatism, 24:60- 63, 1981.

Veintiséis (26) pacientes con Lupus Eritematoso sistémico parcialmente controlado con 30 mg diarios de prednisona o menos, fueron seleccionados para recibir Levamisole 150 mg semanal o placebo. Muchos pacientes demostraron agravamiento de la enfermedad después de seis meses de tratamiento y muchos requirieron aumento de la dosis del esteroide. Aquellos que estaban en Levamisole no estuvieron mejor que aquellos que estaban en placebo.

Ramón E. Ortiz, MD

HEAD TRAUMA IN CHILDREN: WHEN IS A ROENTGENOGRAM NECESSARY: J.C. Leonidas, M.D., W. Ting, M.D., A Binkiewicz, M.D.,R. Vaz, M.D., R. Michael Scott, M.D. and S.G. Pauker, M.D.; Pediatrics 69:2: 1980

The value of routine skull roentgenography for head trauma has been questioned in a number of publications during the last ten years. Skull roentgenograms are rarely positive after trauma to the head, especially in children, and only in a small number of cases in management affected by skull X ray.

Review of 354 infants and children who had skull roentgenography for head trauma over a 2 1/2 year period revealed a low incidence of fractures (4.2%) and no seriuos intracraneal complication.

The author proposed criterias for skull X rays of children with head trauma which included infants less than 1 year, unconsciousness of less than 5 minutes, gun shot wound of skull, previous craniotomy with shunting tube in place, palpable hematoma on scalp, skull depression, CSF discharge from ear or nose, blood in middle ear, Battle sign, Racoon's eye, lethargy, coma or stupor and focal neurological signs.

The application of these criteria will increase predictive value of a positive result to 93.7%.

Nevertheless the clinical importance of detection of skull fractures remains uncertain.

Marta Valcárcel, MD

URINARY TRACT INFECTIONS IN YOUNG INFANTS: Charles M. Ginsburg, M.D. and George McCracke, Jr., M.D.; Pediatrics 69:4: 1982

Data is presented on 100 young infants aged 5 days to 8 months hospitalized with their first known acute urinary tact infection.

In this study male infants accounted for the majority of urinary tract infections in the first three months of life, but female infants predominated thereafter.

Sepsis was documented in 31% of neonates, 21% of infants aged 1 to 2 months, 14% of those age 2 to 3 months and 5.5 of infants 3 months of age.

Roentgenographic abnormalities of the urinary system were found in 45% of female and 7% of male infants.

All infants responded promptly to antimicrobial agents which consisted on administration of gentamycin and ampicillin or gentamycin alone. Either regimen was effective as initial antimicrobial therapy in young infants with urinary tract infections.

Marta Valcárcel, MD

DIAGNOSTICO DE EFUSION PLEURAL CON ANALISIS DEL CROMOSOMA: Falor WH, Chest 1982, 81(2) p. 193

El estudio se diseña para comprobar las potencialidades diagnósticas de dos métodos de examen de las efusiones pleurales: a) el examen citológico usual usando la técnica Papanicolau b) el análisis cromosómico.

Se estudiaron 60 pacientes con efusiones pleurales sin diagnóstico. Se aspiraron las efusiones y se sometieron a un análisis doblemente ciego de ambos métodos.

El estudio encontró 33 efusiones relacionadas con un tumor maligno y 27 efusiones asociadas con enfermedades no-neoplasicas de el pulmón, corazón o hígado.

El análisis cromosómico diagnosticó el 91% de las efusiones malignas mientras que la citología pudo diagnosticar solamente el 64% de ellas. La gran diferencia en posibilidades diagnósticas ocurrió en fusiones debidas a carcinomas intratorácicos en las cuales la citología usual fue positiva en el 39% de los casos y el análisis de cromosomas diagnosticó el 89% de las veces.

En los casos de efusiones benignas la citología usual estuvo correcta en todas mientras que el análisis de cromosoma fue falsamente positivo en 2 de los 27 casos.

El examen citogenético de las efusiones pleurales demuestra anormalidades tanto numéricas como morfológicas incluyendo los "cromosomas marcados". Una efusión se consideraba maligna si había un cromosoma "marcado" o si 10% o más de los metafases estudiadas eran hiperdiploides.

En resumen, el análisis de cromosomas de células halladas en las efusiones pleurales ofrece mucha más certeza que los métodos citológicos usuales en el diagnóstico de efusiones pleurales.

Ramón Figueroa Lebrón, MD

AMERICAN COLLEGE OF PHYSICIANS

The American College of Physicians' Board of Regents announced approval of four new **Clinical Efficacy Assesment Program (CEAP)** recommendations. They are:

I Hyperbaric oxygen therapy in treament of arthritis. The ACP endorses the Arthritis Foundation's recommendation that, at the present time, hyperbaric oxygen therapy is an unacceptable form of treatment for any known form of arthritis. Although there are metabolic changes in joints of individuals with inflammatory arthritis, particularly rheumatoid arthritis, which include low oxygen tension, increased levels of metabolites and elevated CO^2, it is unclear whether such changes aggravate the condition. Data from studies on the use of huperbaric oxygen in treating inflammatory arthritis suffer from lack of proper controls and the inability to extrapolate results in animal models to humans.

II Percutaneous transluminal coronary angioplasty (PTCA) is an investigational procedure. The immediate efficacy and safety of the procedure is not established. Follow-up data are inadequate to make any meaningful conclusions regarding long term complications and efficacy. It is not known what medical therapy should be utilized after the procedure is performed.

Candidates for PTCA should have intractable angina inadequately controlled with maximal medical therapy; objective evidence of myocardial ischemia; normal ventricular function; and proximal discrete, accessible, noncalcific, segmental, high-grade obstruction of a coronary vessel. More effort must be made to collect adequate clinical, hemodynamic, and angiographic data in all patients prior to the procedure and to obtain systematically clinical and angiographic follow-up on such patients following the procedure. These efforts will be best coordinated by the National Heart, Lung and Blood Institute registry, in which the College encourages physicians performing PTCA to participate, tne by the adoption of multicenter, randomized clinical trials.

III Intravenous histamine has not been shown to be an effective treatment for Meniere's acute and sudden hearing loss, and headache. Indeed, there is evidence that histamine may provoke headaches. Intravenous histamine may produce palpitations, tachycardia, and syncope. Patients with decreased cardiac output or reduced perfusion to essential organs are at particular risk from intravenous histamine induced alterations in cardio-vascular function. In addition, it is unclear whether repeated intravenous histamine might produce some of the severe symptoms of mastocytosis which are thought to be due to histamine release.

The CEAP study evaluates the clinical efficacy of nonsurgical laboratory tests and procedures to determine outmoded tests and encourage newer, more accurate replacements for them.

AMERICAN ACADEMY OF PEDIATRICS

YOUNGER CHILDREN IN SPECIAL DANGER FROM DOG BITES, STUDY SAYS

The number of dog bites has increased in recent years and children are the most frequent victims, according to research reported in **Pediatrics,** the journal of the American Academy of Pediatrics.

The research team was headed by Yoon-Taek Chun, M.D., FAAP, and Jay E. Berkelhamer, M.D., FAAP. Its work was based on all visits to the University fo Chicago's Wyler Children's Hospital emergency room in 1979.

With the rising crime rate, more people are buying or even renting large and sometimes vicious dogs to protect their family or property. One problem, according to the researchers, is that children under age four are particularly defenseless, receive the most serious injuries, and usually have not been warned about the dangers of dogs.

Even family pets can unknowingly be provoked by small children. In fact, the reserach team's review of 114 of 199 dog bite victims showed that 90 percent of chilcren under four were bitten at home, while parents were present, and 47 percent were bitten by their own dogs.

Of the 114 victims, 19 were under four and 95 were between four and sixteen. The researchers found several differences in how children in the two age groups were bitten by dogs.

Of the 114 victms, 19 were under four and 95 were between four and sixteen. The researchers found several differences in how children in the two age groups were bitten by dogs.

The researchers found that even dogs previously thought of as "gentle" can be provoked into an attack by an unknowing youngster. Eighty-five percent of the younger children were bitten by dogs who had not bitten anyone before; only 50 percent of the older victims were bitten by this type of dog. With only sixteen percent of the younger children warned about the dangers of dogs before being bitten, as opposed to 57 percent of the older group, it would appear youngsters' special vulnerability stems at least in part from naivete about their pets.

Perhaps most important, the researchers say, is the fact that younger children usually receive the most serious dog bite injuries —those on the upper part of their bodies. Sixty-three percent of the younger children were bitten on the head, face or neck; only 18 percent of the older group were bitten in this area.

To prevent dog bites to younger children, the researchers suggest that parents delay adopting dogs as pets until children are older. It is difficult, the research team says, to teach younger children how to recognize potential conflicts with a family pet. If dogs are brought into the home, the researchers urge that "utmost care must be taken by parents at all times."

SAFETY CAPS EFFECTIVELY PREVENT CHILD POISONING, STUDY REPORTS

Almost 200,000 children escaped accidental poisoning during a six-year period because a federal law requieres that a variety of consumer products and medicines have "child-proof" closures, a newly published study reports.

Results of the study appear in the March issue of **Pediatrics,** the journal of the American Academy of Pediatrics (AAP).

The study is the first research designed to estimate how effectively the Poison Prevention Packaging Act of 1970 has decreased the rate of poisoning of children under five, and was prepared by William W. Walton , Ph.D., of the Consumer Product Safety Commission, Washington, D.C. The AAP was one of the leading organizations concerned with children's health which sought pasage of the Act.

Walton's research analyzed poisoning trends in the period 1973 to 1979, when most of the Act's regulations governing packaging of 15 substances went into effect. Data were reported by statistically selected hospitals with emergency rooms.

To determine the number of poisonings prevented by the Act, Walton computed the rate at which children under five were poisoned by products and drugs requiring the special closures. This figure was compared to the rate at which children were poisoned by substnces not covered by the Act. Walton made adjustments to control for such factors as the declining number of children under five during the six-year period.

Had the Act not been passed, Walton's comparisons indicate taht over 190,000 additional chldren would have been poisoned during the six-year period, and the poisoning rate in 1978 would have been about 6.2 for every 1,000 children.

Instead, the study found that a dramatic decline tood place in both the total number and the rate of poisonings by substances covered under the Act. The number of poisonings decreased from 95,000 in 1973 to 52,000 in 1978, a delcine of about 45 percent. The rate per 1,000 children decrased from 5.7 to 3.4

Walton also notes there was a decline in the death rate due to accidental poisoning of children during the six-year period, from about 1.1 per 1,000 children in 1973 to o.5 in 1978. While the decline in deaths began before the Act went into effect and the use of child restraint containers "are but one factor that could be responsible for this significant delcine, they have undoubtedly been an important one," according to Walton.

To further reduce the numbver of children accidentally poisoned, Walton suggests that parents be educated on the dangers of drugs and other products commonly found in the home. Instituting further regulations probably would be of little value, he says, since the substances which cause most of the accidental poisonings already are covered by the Act.

AMERICAN COLLEGE OF SPORTS MEDICINE

The American College of Sports Medicine Annual Meeting will be held May 26-29 in Minneapolis, Minnesota at the Minneapolis Auditorium and Convention Hall. There will be over 350 scientific papers presented along with 13 half-day symposia, 9 evening colloquia, and over 100 technical exhibits. Dr. George A. Bray from the University of Southern California will be the featured speaker at the J.B. Wolffe Memorial Lecture which will start the program on Wednesday, May 26 at 1:00 p.m.

Registration for the conference in $80 for members and $100 for non-members. Information on the annual meeting is available by writing to ACSM, 1440 Monroe Street, Madison, WI 53706 or by calling (608) 262-3632.

CARDIO 82
Asociación Puertorriqueña del Corazón

SESION CIENTIFICA
5 y 6 de septiembre de 1982, Dorado Beach Hotel

La Asociación Puertorriqueña del Corazón tiene el placer de anunciar su próxima actividad científica anual - CARDIO-82 - con la participación de distinguidos cardiólogos visitantes en colaboración con cardiólogos locales. Esta actividad, co-auspiciada por la División de Educación Médica Continuada de la Escuela de Medicina de la Universidad de Puerto Rico, se llevará a cabo en el Hotel Dorado Beach los días 5 y 6 de septiembre de 1982.

Serán dos días de actualización en cardiología durante los cuales se discutirán los siguientes tópicos: Fallo Cardíaco/ Nuevos Avances Diagnósticos en Enfermedades Cardiovasculares incluyendo Cardiología Pediátrica/ Arritmias/ Marcapasos/ y Cirugía Vascular

Compartirán con nosotros figuras tales como:
Carlos de Castro, Houston, Texas
Peter Gazes, Charleston, South Carolina
Thomas P. Graham, Nashville, Tennessee
Jay W. Harthorne, Boston, Massachusetts
Julio E. Pérez, Saint Louis, Missouri
Jesse E. Thompson, Dallas, Texas

Los asistentes al curso recibirán doce (12) horas-crédito en Categoría I.

Próximamente se le enviará el programa, blancos de matrícula y registro del hotel.

Para mayor información puede comunicarse con la Asociación Puertorriqueña del Corazón: 763-8275, 751-6595 y 759-8410 ó con la División de Educación Médica Continuada de la Escuela de Medicina.

M. Etienne Otaño, M.D.
Presidente
Asociación Puertorriqueña del Corazón

Carlos E. Girod, M.D.
Presidente
Comité de Asamblea Anual

Legislaciones de Salud

CAMARA DE REPRESENTANTES

Proyecto de la Cámara 298*, radicado por la Minoría. — Aprobado en la Cámara el 24/2/82 y enviado al Senado el 1/3/82. — Para adicionar un nuevo párrafo (31) al apartado (b) de la Sección 22 de la Ley Núm. 91, aprobada en 29 de junio de 1954, según enmendada, conocida como "Ley de Contribuciones sobre Ingresos de 1954" a los fines de proveer que las aportaciones de un patrono a planes de enfermedad o accidente como compensación (mediante seguro o en otra forma) a sus empleados por lesiones personales o enfermedad estarán excluidos del ingreso bruto del empleado.

*Nueva Legislación o cambio de status.

Proyecto de la Cámara 3234, radicado por el Rep. Navarro Alicea. — Comisión de Gobierno. — Para reglamentar la práctica de las profesiones de tecnólogos en Medicina Nuclear y Técnico en Medicina Nuclear en el Estado Libre Asociado de Puerto Rico, crear la Junta Examinadora de Tecnólogos en Medicina Nuclear y Técnicos en Medicina Nuclear; establecer sus facultades y obligaciones por violaciones a esta ley.

Proyecto de la Cámara 324, radicado por el Rep. López Galarza. — Comisiones de Gobierno y Salud y Bienestar. — Para enmendar la sección 14-102 de la Ley Núm. 141 de 20 de julio d e1960, según enmendada, a fin de que queden exentos del pago de peaje las ambulancias del Gobierno del Estado Libre Asociado de Puerto Rico cuando se encuentren en funciones oficiales, transportando pacientes o personas afectadas por alguna condición física".

Proyecto de la Cámara 370, radicado por el Rep. Torres Velázquez. Comisión de Salud y Bienestar. —Para adicionar un nuevo inciso y reenumerar el inciso 14del Artículo 6d ela Ley Núm. 11 de 23 de junio de 1976, según enmendada, conocida como "Ley de Reforma Integral de los Servicios de Salud de Puerto Rico", a los efectos de disponer que el Consejo Coordinador de Salud recomiende al Secretario de Salud la reglamentación que estime necesaria para garantizar la plena prestación de servicios médicos de emergencia en facilidades privadas, sin discrimen de clase alguna, y para disponer sobre la promulgación de esa reglamentación.

Proyecto de la Cámara 324, radicado por el Rep. Colberg Ramírez. — Comisiones de Salud Bienestar y de Gobierno. —Para disponer la organización del Colegio de Médicos-Cirujanos de Puerto Rico, especificar sus funciones, deberes y fijar penalidades por infracciones a las mismas.

Proyecto de la Cámara 422, radica por el Rep. Samuel Ramírez. — Comisiones de Salud y Bienestar y de Gobierno. —Para enmendar el inciso (2) del Artículo 4 y el Artículo 5 de la Ley Núm. 152 del 3 de junio de 1976, que regula el ejercico de la profesión de Optico y Técnico de Laboratorio de Optica a los fines de sustitur varios requisitos que determinan jla concesión de licencias que autorizan el ejercicio de la práctica de la óptica.

Proyecto de la Cámara 436*, radicado por el Rep. Cepeda García. — Comisiones de Salud y Bienestar y de Asuntos del Consumidor. —Para adicionar un cuarto párrafo a la Sección 8 y añadir incisos (4) y (5) de la ley Núm. 97 de 24 de junio de 1971, según enmendada, y para enmendar la Sección 12 de la Ley Núm. 75 de 12 de agosto de 1925, según enmendada, con el fin de que los consumidores puedan escoger si desean mandar a hacer sus dentaduras o dientes artificiales directamente al técnico dental o denturista, y por ello eliminamos toda restricción que hasta ahora lo impedía.

*Nueva Legislación o cambio de status.

Proyecto de la Cámara 441*, radicado por el Rep. Vélez Acevedo. — Comisiones de Salud y Bienestar. —Para enmendar el inciso (p) del Artículo 5 de la Ley núm. 26 de 13 de noviembre de 1975, según enmendada, conocida como "Ley de Administración de Facilidaes y Servicios Hospitalarios de Salud de Puerto Rico", a fin de requerir de dicha Administración que mantenga un récord de las personas naturales o jurídicas a quienes se les haya otorgado o se les otorgue algún contrato de serivicios en las facilidades hospitalarias del Departamento de Salud.

Proyecto de la Cámara 442*, radicado por el Rep. Vélez Acevedo. — Comisiones de Salud y Bienestar. — Para autorizar al Secretario de Instrucción Pública y al Secretario de Salud a contratar a fin de que el Departamento de Instrucción Pública absorba el pago del salario dejado de percibir por cierto personal del Departamento de Salud a quienes se les ha reducido la jornada de trabajo por insuficiencia de fondos en este último departamento.

Proyecto de la Cámara 443*, radicado por el Rep. Vélez Acevedo. — Comisiones de Salud y Bienestar. —Para reglamentar la práctica de la Terapia Respiratoria, crear la Junta Examinadora de Tecnólogos de Terapia Respiratoria; especificar sus poderes, deberes y facultades; fijar penaldiades y asignar fondos.

*Nueva Legislación o cambio de status.

Proyecto de la Cámara 324*, radicado por el Rep. Vélez Acevedo. — Comisiones de Salud y Bienestar. —Para enmendar el inciso (2) del Artículo 4 y el Artículo 5 d ela Ley Núm. 152 del 3 de junio de 1976 que regula el ejercicio de la profesión de Optico y Técnico de Laboratorio de Optica a

los fines de sustitur varios de los requisitos que determinan la concesión de licencias que autorizan el ejercicio de la práctica de la óptica.

Proyecto de la Cámara 445*, radicado por el Rep. Vélez Acevedo. — Comisiones de Salud y Bienestar. —Para enmendar la Ley 80 del 26 de junio de 1964 con el propósito de actualizar y delimitar de manera más precisa el alcance de lo de que constituye práctica ideal e ilegal de la optometría en Puerto Rico.

Proyecto de la Cámara 463*, radicado por el Rep. Viera Martínez. — Comisiones de Salud y Bienestar y de Gobierno. —Para enmendar el Inciso (2) del Artículo 4 y el Artículo 5 d ela Ley Núm. 152 del 3 de junio de 1976 que reglamenta el ejercicio de la profesión de Optico y Técnico de Laboratorio de Optica, a los fines de sustituir varios de los requisitos que determinan la concesión de licencias que autorizan el ejercicio de la práctica de la óptica.

***Nueva Legislación o cambio de status.**

Proyecto de la Cámara 471*, radicado por la Minoría.— Comisiones de Salud y Bienestar. —Para enmendar las secciones 3-100 del ARtículo 1 Capítulo III; 3-601 y 3-609 del Artículo 8 Capítulo III; y 3-706 del Artículo 7 Capítulo III de la Ley Núm. 116, del 12 de junio de 1980 que establece el Código de Salud Mental de Puerto Rico, para que el Tribunal señale una vista en aquellos casos en que la persona haya sido admitida involuntariamente a una facilidad de salud mental.

Proyecto de la Cámara 472*, radicado por la Minoría.— Comisión de Gobierno. —Para enmendar el Artículo 511A; adicionar un Artículo 511B; adicionar un último párrafo al inciso (c) y enmendar los apartados (1) y (3) del inciso (e) del Artículo 512 de la Ley Núm. 4, de 23 de junio de 1971, según enmendada, conocida como Ley de Sustancias Controladas de Puerto Rico, para conferir a los inspectores d ela División para el control de Drogas y Narcóticos las facultades correspondientes a un agente del orden público y para otros fines.

Proyecto de la Cámara 473*, radicado por la Minoría. Comisiones de Gobierno. —Para enmendar el inciso (b) de la sección 7, de la Ley Núm. 95, de 29 de junio de 1963, según enmendada, para disponer que cuando ambos cónyuges sean empleados públicos tendrán derecho a que se le apliquen las aportaciones gubernamentales de ambos al plan de salud famiiar, hasta el máximo de la referida aportación gubernamental.

***Nueva Legislación o cambio de status.**

Proyecto de la Cámara 498*, radicado por el Rep. Vélez Acevedo. — Comisiones de Salud y Bienestar. —Para actualizar y delimitar el alcance de la práctica de ciertas profesiones como la Quiropráctica. Estas enmiendas pretenden poner al día los requisitos educativos necesarios para practicar la Quiropráctica en Puerto Rico con un nivel mayor de excelencia profesional.

Proyecto de la Cámara 506*, radicado por el Rep. Calero Bermúdez. —Comisiones de Gobierno y Salud y Bienestar. —Para enmendar el título, los Artículos 1, 2 y 3 (ahora reenumerados a 3 y 4); los Incisos (b), (c) y (d) del ARtículo 4 (ahora reenumerado 5); los Artículos 6 al 10, 13 y 14 (ahora reenumerados 14 y 15) y los Artículos 16 y 19 (ahora reenumerada 17 y 19). Se añade un Artículo 2. todos los demás Artículos se reenumerarán del 2 al 18 coo 3 al 19 repectivamente, de la Ley Núm. 78 de 24 de junio de 19 1963, según enmendada, que reglamentará el ejercicio de la tecnología radiológica.

Proyecto de la Cámara 513*, radicado por el Rep. Torres Velázquez. — Comisión de Gobierno. —Para crear la Corporación de Empresas de Ciudadanos Impedidos, adscrita al Departamento de Servicios Sociales.

***Nueva Legislación o cambio de status.**

Proyecto de la Cámara 514*, radicado por el Rep. Torres Velázquez. — — Comisiones de Salud y Bienestar y Bienestar y Gobierno. —Para enmendar el inciso (b) de la Sección 8 de la Ley Núm. 95 de 29 de junio de 1963, según enmendada, conocida como "Ley de Beneficios de Salud para Empleados Públicos" a los efectos de autorizar a que los cónyuges puedan acogerse a un mismo plan d esalud cuando ambos sean empleados públicos, percibiéndose para el mismo plan las aportaciones patronales correspondientes a ambos cónyuges".

Proyecto de la Cámara 545*, radicado por el Rep. Vélez Acevedo. — Comisión de Hacienda. —para enmendar el inciso 91) del apartado (a) del Artículo 51 de la Ley Núm. 2 de 20 de enero de 1956, según enmendada, a los fines de eximir del pago de impuestos los artículos para facilitar la locomoción individual de inválidos, ciegos, lisiados o cardiacos y todo equipo ortopédico para uso de impedidos.

Proyecto de la Cámara 551*, radicado por el Rep. Rony Jarabo. — Comisiones de Salud y Bienestar. —Para adicionar el Capítulo VII, Artículo 12 y renumerar Capítulo VII, Artículo 12, 13, 14 y 15 y el Capítulo VIII, Artículos 16 y 17 de la Ley Núm. 243 de 15 d emayo de 1938, según enmendada, a los fines de establecer la adopción de un sello especial para ser adherido a cada receta y envase de un medicamento prescrito y para otros fines.

***Nueva Legislación o cambio de status.**

Proyecto de la Cámara 552*, radicado por el Rep. Viera Martínez. — Comisiones de Salud y Bienestar. —Para ordenar al Secretario de Salud del Estado Libre Asociado de Puerto Rico el establecimiento y operación de Refugios Regionales de Animales, fijarle pautas y asignarle fondos.

SENADO

Proyecto del Senado 401, radicado por la Senadora Goyco, Ana Nisi. Comisión de Salud y Calidad Ambiental. — Para enmendar el Artículo 4 de la Ley Núm. 79 de 28 de junio de 1978, para incluir a los patólogos del habla-lenguaje, audiólogos y terapeutas del habla en las profesiones relacionadas con la salud que deben practicar por un período de un año en el servicio público y que se provee en esa ley.

Proyecto del Senado 427, radicado por la Senadora Goyco, Ana Nisi. — Comisión de Salud y Calidad Ambiental. —Para enmendar el Capítulo II, Artículo 3, el Capítulo III, Artículos 5 y 7 de la Ley Núm. 243 de 15 de mayo de 1938, según enmendada, con el fin de incluir como miembros del Colegio de Farmacéuticos a los farmacéuticos que cumplan el requisito de un año de servicio público.

Proyecto del Senado 465, radicado por los Senadores Rivera Ortiz, G. y Goyco, Ana Nisi. — Comisión de Salud y Calidad Ambiental y de Gobierno. —Para enmendar el título, y los Artículos 1, 2, 3 y 5 de la Ley Núm. 79 de 28 de junio de 1978, a fin de transferir a una Junta Especial de Profesiones de la Salud las funciones que ahora desempeña el Secretario de Salud en virtud de la referida ley.

Proyecto del Senado 466, radicado por los Senadores Rivera Ortiz, G. y Goyco, Ana Nisi. — Comisión de Salud y Calidad Ambiental y de Gobierno. —Para enmendar los Artículos 2, 6, 10 y el Inciso (6) del Artículo 13 de la Ley Núm. 22 de 22 de abirl de 1931, según enmendada, a fin de facilitar el ejercicio de las facultades y deberes del Tribunal Examinador de Médicos.

Proyecto del Senado 480, radicado por el Senador Rivera Ortiz, G. — Comisión de Salud y Calidad Ambiental y De lo Jurídico. —Para derogar la Ley Núm. 90 de 22 de junio de 1967, que reglametna la profesión de Tecnología Médica en Puerto rico y actualizarla a tenor con los conocimientos científicos Médicos: disponer sobre sus deberes y facultades: establecer penalidades por violaciones a esta ley; y para otros fines.

Proyecto del Senado 498, radicado por el Senador Ríos Ruiz. — Comisión de Salud y Calidad Ambiental, De lo Jurídico y de Gobierno. —Para disponer la organización del Colegio de Médicos-Cirujanos de Puerto Rico, especificar sus funciones, deberes y fijar penalidades por infracciones a las mismas.

Proyecto del Senado 511*, radicado por la Senadora Goyco. —Comisión De lo Jurídico. —Las siguientes enmiendas se proponen a los fines de atemperar la Ley Núm. 80 de 26 de junio de 1964, según enmendada, a las disposiciones de la Ley Núm. 11 de junio de 1976, según enmendada, que provee para la renovación de licencias cada tres (3) años a través de la educación continua y para el registro de profesionales de la salud.

Proyecto del Senado 514*, radicado por el Senador Nogueras (Hijo). Comisiones De lo Jurídico y Salud y Calidad Ambiental. —Para enmendar las Secciones 3-100 del ARtículo 1 Capítulo III; 3-601 y 3-609 del Artículo 6 Capítulo III; y 3-706 del Artículo 7 Capítulo III, de la Ley Núm. 116, del 12 de junio de 1980 que establece el Código de Salud Mental de Puerto Rico, para que el Tribunal señale una vista en aquellos casos en que la persona haya sido admitida involuntariamente a una facilidad de salud mental.

Proyecto del Senado 536, radicado por el Senador Rivera Ortiz, G. — Comisiones de lo Jurídico y Salud y Calidad Ambiental. —Para eximir que todas las medicinas, medicamentos y productos médicos o paramédicos que se ofrezcan en venta en Puerto Rico lleven consigo en el idioma español el contenido de la medicina, medicamento o producto, la forma de administrarlo o usarlo y cualesquiera otros datos que deba conocer el consumidor; y para fijar penalidades.

Proyecto del Senado 536, radicado por el Senador Rivera Ortiz, G. — Comisiones de Gobierno y de Salud y Calidad Ambiental. —Para adicionar un cuarto párrafo a la Sección I; enmendar la Sección 5; enmendar la Sección 8 y añadir incisos (4) y (5) d ela Ley Núm. 97 de 24 de junio de 1971, según enmendada, y para enmendar la Sección 12 d ela Ley Núm. 75 de 12 de agosto de 1925, según enmendada que reglamenta la práctica de los técnicos dentales con el fin de que los consumidores puedan escoger si desean mandar a hacer sus dentaduras o dientes artificiales directamente al técnico dental o denturista, y por ello eliminamos toda restricción que hasta ahora lo impedía.

Proyecto del Senado 536, radicado por el Senador Goyco, Ana Nisi. — Comisiones De lo Jurídico, Salud y Calidad Ambiental y de Instrucción. —Para adicionar un nuevo Art. 1, enmendar y redesignar como los Arts. 2, 3, 4, 5, 6, 7, 8, 9, 10 y 11 los Arts. I, 2, 3, 4, 5, 6, 7, 8, 9 y 10, adicionar un nuevo Art. 12 y redesignar como Art. 13 el Art. 1 de la Ley Núm. 148 de 4 de julio de 1975, según enmenda, que creó la Junta Examinadora de Educadores en Salud a fin de autorizar y reglamentar, en adición al ejercicio de la profesión de educador en salud, el ejercicio de la profesión de educador en salud comunal, conformar las disposiciones de esta ley con la legislación vigente en el campo de la salud y fijar penalidades.

Proyecto del Senado 545, radicado por la Senadora Goyco, Ana Nisi. Comisiones de Gobierno y de Instrucción. —Para autorizar al Secretario de Instrucción Pública y al SEcretario de Salud a contratar a fin de que el Departamento de Instrucción Pública absorba el pago del salario dejado d epercibir por cierto personal del Departamento de Salud a quienes se les ha reducido la jornada de trabajo por insuficiencia de fondos en este último departamento.

Proyecto del Senado 546, radicado por la Senadora Goyco, Ana Nisi. — Comisiones de Gobierno y de Instrucción. — Para adicionar los incisos D y E al Artículo 2; adicionar el inciso (7) al apartado (b) del Artículo 8; enmendar el Artículo 9; y derogar el Artículo 11 de la Ley Núm. 31 de 30 de mayo de 1975, según enmendada, con el fin de que la administración de servicios de salud debe ser ejercida sólo por los profesionales adiestrados y licenciados para ello, definido el ejercicio de esta profesión en su función de las labores realizadas y no meramente por el nombre que se utilice para designar un puesto.

Proyecto del Senado 547*, radicado por el Senador Nogueras (Hijo). — Enviado a la Cámara 21/4/82. —Para enmendar el inciso (b), de la sección 7, d ela Ley Núm. 95, de 29 de junio de 1963, según enmendada, para disponer que cuando ambos cónyuges sean empleados públicos, tendrán derecho, a que se le apliquen las aportaciones gubernamentales de ambos al plan de salud familiar, hasta el máximo de la referida aporación gubernamental.

*Nueva Legislación o cambio de status.

Proyecto del Senado 551, radicado por el Senador Nogueras (Hijo). — Comisiones De lo Jurídico y Gobierno. —Para enmendar el Artículo 511A; adicionar un Artículo 511B; adicionar un último párrafo al inciso (c) y enmendar los apartados (1) y (3) del inciso (e) del Artículo 512 de la Ley Núm. 4, de 23 de junio de 1971, según enmendada, conocida como Ley de Sustancias Controladas de Puerto Rico, para conferir a los inspectores d ela División para el control de Drogas y Narcóticos las facultades correspondientes a un agente del orden público y para otros fines.

Proyecto del Senado 558, radicado por la Senadora González Modestti. — Comisiones de Salud y Calidad Ambiental y Gobierno. —Para reglamentar la Enfermería Práctica en puerto Rico, para crear una Junta Examinadora, para disponer sobre la colegiación de las Enfermeras Prácticas; fijarle deberes y conferirle facultades.

Proyecto del Senado 564, radicado por el Senador Cruz Martínez. — Para enmendar el inciso 9a) de la SEcción 8 de la Ley Núm. 95 de 29 de junio de 1963, según enmendada, conocida como "Ley de Beneficios de Salud para Empleados Públicos", a los fines de aumentar la aporación patronal del Gobierno para los beneficios de salud de los empleados del mismo.

Proyecto del Senado 569, radicado por la Senadora González Modestti. — Comisiones De lo Jurídico y de Instrucción. —Para enmendar los Arts. 2, 3 y 8 de la Ley Núm. 21 del 22 de julio de 1977 a ifn de definir más claramente los derechos bajo esa ley del niño impedido y armonizar las disposiciones de la ley con la Ley Federal de Educación para todos los Niños Impedidos (PL 94-142) según enmendada y su reglamento.

Proyecto del Senado 596, radicado por la Senadora Goyco, Ana Nisi. — Comisión De lo Jurídico. —Para adicionar un cuarto párrafo a la Sección 1; enmendar la Sección 5; enmendar la Sección 8 y añadir incisos (4) y (5) de la Ley Núm. 97 de 24 de junio de 1971; según enmendada, con el fin de que los consumidores puedan escoger si desean mandar a hacer sus dentaduras o dientes artificiales directamente al técnico dental o denturista, y por ello eliminamos toda restricción que hasta ahora lo impedía.

Proyecto del Senado 597, radicado por la Senadora. — Comisiones de Salud y Calidad Ambiental y De lo Jurídico. —Para atemperar la actual ley que reglamenta el ejercicio de la profesión profesión de Terapia Física en Puerto Rico y ponerla a tono con los conocimientos modernos y competencias profesionales en este campo de la salud.

Proyecto del Senado 600, radicado por la Senadora Goyco, Ana Nisi. Comisión de Salud y Calidad Ambiental. —Para designar el mes de abril de cada año como el "Mes de la Prevención y el control de Cáncer" en Puerto Rico.

Proyecto del Senado 608*, radicado por el Senador Méndez Justo A. — Comisiones De lo Jurídico y de Salud y Calidad Ambiental. —Para enmendar las Secciones 13 y 13-A de la Ley Núm. 75 de 8 d eagosto de 1925, según enmendada, que crea la "Junta Dental Examinadora", a fin de establecer unas penalidades más severas por el ejercicio ilegal de la odontología.

Nota: Copia de estos proyectos en su totalidad están disponibles para quienes así lo soliciten por correo a la Asociación Médica de Puerto Rico.

ANSWERS TO THE QUIZ:

1. c

1. c	7. a
2. e	8. d
3. d	9. c
4. b	10. b
5. a	11. c
6. c	12. b

See: The immunocompromised Patient: Guidelines for the Clinical Approach.

AMA NEWS

JOGGING SAFE FOR WOMEN AFTER CHILD-BIRTH

Most women can safely resume their regular jogging or exercise program after childbirth, according to two physicians writing in the Journal of the American Medical Association.

Many women are concerned about incurring a prolapsed ("fallen") uterus during strenous exercise after pregnancy. According to Edward C. Hill, M.D., however, a prolapse, or downward displacement, of the organ is almost always a result of uterine ligaments weakened in chilbirth. If a woman has not sustained any injury to the supporting tissues of the pelvis during childbirth, she is not predisposed to uterine prolapse, and activities such as jogging will not be detrimental, says Hill, who is a member of the faculty of the University of California School of Medicine, San Francisco.

"There is also no indication that jogging worsens an already present uterine prolapse," adds Christine E. Haycock, M.D., Associate Professor of Surgery at the New Jersey Medical School, Newark. "Factors such as obesity and lack of good muscle tone probably contribute more to uterine prolapse than any form of exercise, including jogging."

Both physicians agree that a gradual resumption of exercise is advisable after delivery. Regardless of her past activity, says Dr. Haycock, the returning runner should proceed like any other beginner, starting with a ten to 15-minute stretching routine before jogging. Before doing any distance running, she should alternate between walking and jogging until she reaches her original condition.

The muscle tone and position of the uterus should return tonormal within six weeks of delivery, according to Dr. Hill, and that is when a new mother can safely resume her exercise program.

STUDY SUGGESTS TOO MANY PATIENTS ADMITTED FOR INTENSIVE CARE

Most of us think of intensive care units in hospitals as the place where the most seriously ill patients —people we picture as being close to death— are surrounded by machines and given around-the-clock attention, the kind of care associated with life-saving situations. That may not be entirely accurate according to a study published in **JAMA.**

Dr. William A. Knaus at George Washington University Medical Center in Washington, D.C., reported that nearly half the patients admitted to his hospital's ICU over an eight-month period actually did not need intensive treatment. Instead, these patients mainly needed close nursing attention with the emphasis on observation, and this, Dr. Knaus suggests, could have been accomplished elsewhere in the hospital rather than in the costly ICU.

The implication of this study, if the same pattern holds true nationally, is that admissions to ICUs conceivable could be cut back without jeopardizing patient care and this, in turn, would slow the demand for more ICU beds, which have been increasing at about four percent a year.

In 1960, only 10 percent of U.S. hospitals with more than 200 beds had ICUs. Now 99 percent of these hospitals have such facilities, and it is estimated that some 42,000 patients a day are in an intensive care units. Traditionally, Dr. Knaus said, it has been assumed that these patients require "a costly level of therapeutic intervention and have a high in-hospital mortality." He and his colleagues, who conducted the study on 624 consecutive admissions to the ICU, found a far different situation. About half of the patients admitted were not in any immediate danger; in other words their vital signs were stable, and they received only minimal amounts of active treatment.

Other studies, Dr. Knaus pointed out, have shown that for every patient admitted to the ICU not needing intensive treatment, an experienced ICU nurse is being under-utlized.

With emphasis lately on improving the cost-effectiveness of medical care, Dr. Knaus said that it is appropriate to take a closer look at who is being admitted to ICUs. Substantial savings could occur if only essential requests for ICU admissions are made.

CARDIOVASCULAR MORTALITY IN STRONG DECLINE

A decline in cardiovascular mortality since 1968, especially in deaths from coronary heart disease, proves that cardiovascular diseases are not an inevitable consequence of aging or genetic makeup and can be prevented, writes William B Kannel, MD, in **JAMA.**

Kannel, who is Professor of Medicine and Chief of Preventive Medicine and Epidemiology, Boston University Medical Center, speculates that a reduction in the incidence and severity of cardiovascular diseases may be a reason for the decline in mortality —and that preventive measures and life-style changes could be contributing factors.

The are-adjusted cardiovascular death rates fell 25 percent in the decade ending in 1979, Kannel said, and the decline seems to be continuing.

About 42 percent of the decline in cardiovascular mortality since 1950 was achieved in just five years since 1972. Although lack of incidence data make it impossible to tell whether the decline reflects a reduction in the incidence and severity of disease or an improvement in life expectancy afte an attack, indirect evidence suggests that the former is likely and that attention to cardiovascular risk factors and changes in life-style may be involved, Kannel said.

Evidence for the health benefits to be gained from controling hypertension and stopping smoking is now available from controlled clinical trials, and modification of these risk factors are likely contributors to the decline in cardiovascular mortality. Hypertension-related deaths have shown the steepest decline, and there is a prompt and dramatic decline in sudden death and in death from myocardial infarction after cessation of smoking, Kannel said.

Although hotly debated, overnutrition appears to be the most likely cause for the high blood lipid values so fundamental to the development of atherosclerosis, Kannel said. But the American public has become more aware of the health implications of overnutrition, and coincident with this, Kannel said, cholesterol values have declined along with per capita consumption of milk, cream, butter, eggs and animal fats.

In an editorial accompanying Kannel's article, James A. Schoenberger, MD, argues that, although definitive evidence in favor of modifying cardiovascular disease risk factors is lacking, the strong downward trend in cardiovascular mortality is persuasive enough to convince practitioners to endorse risk reduction programs. Schoenberger is Chairman of the Department of Preventive Medicine, Rush-Presbyterian-St. Luke's Medical Center, Chicago.

According to Schoenberger, there is evidence that the time lag between reduction of risk and benefit to health is shorter than previously thought. He urges physicians to begin early and vigorous intervention against cardiovascular disease risk factors, advocating the following measures:

- dietary restrictions for patients with total blood choleterol levels above 200 milligrams per deciliter;
- control of elevated blood pressure by weight and salt restriction and by drug therapy if necessary to reduce diastolic pressure to 90 millimeters of mercury or lower;
- persistent efforts to convince patients to stop smoking.

In the conclusion to his article, Kannel points out that in England, where scientific skepticism has led to apathy about preventive efforts, cardiovascular mortality figures have remained constant. Among middle-aged men in 1968, the chance of a coronary heart disease death in an American was 40 percent higer than that of an Englishman, while by 1976 the American risk had actualy declined to below that of the English.

The only segments of the English population that have improved their mortality, Kannel notes, are the higher social classes and physicians.

THE HEAVY BURDEN OF LOW BIRTH WEIGHT BABIES

The United States doesn't fare very well in a listing of countries ranked by their infant mortality rates. We could do no better than tie for 16th place in 1979, the most recent year for which we have statistics, placing lower than most of the countries in northern Europe.

This is partly due to differences in the reporting of infant deaths and in the definition of a live birth versus a stillbirth. We frequently report infant deaths through the first 28 days afte birth, while en Europe infant mortality usually is reported only through the first seven days after birth.

Although there is no consensus on the reason for our poor showing —it has never been clear what role medical care, or its lack, plays in it— a likely cause has been traced to the high number of low brith weight babies born into economically deprived families, according to an article in **JAMA**.

That was what J. David Erickson, PhD, at the Centers for Disease Control in Atlanta, Ga., and Tor Bjerkedal, MD, at the University of Oslo's Institute of Hygiene in Norway, found when they compared birth weight and infant mortality data from both countries.

Using figures adjusted for the mortality at each birth weight —instead of comparing overall mortality statistics— they found that babies of the same weight, on average, had lower death rates in the U.S. than in Norway, which ranked fifth internationally in infant mortality in 1977.

What this means, in essence, is that infant care in this country is as good or even better than it is in Norway, but because of the number of low birth weight babies in the U.S. we don't come out all that high in the standings.

This situation, the **JAMA** authors say, is unlikely to change unless the proportion of U.S. babies born at low birth weight is reduced.

In the U.S., mortality for black babies far exceeds that in white babies, the authors wrote. In 1977, for example, mortality among white babies was 12.3 per 1,000 births, while the rate for other races was 21.7. In an international ranking, the authors wrote, the white race would have placed tenth, but the other race rate would not have placed among the first 25v nations.

Research has convincingly shown that smaller babies have a higher risk of early death, as Nigel Paneth, MD, of Columbia University, says in an editorial accompanying the **JAMA** article.

He calls low birth weight America's number one pediatric public health problem, and says that it will not go the way of diphteria and polio without a similar concerted and well-funded effort.

GERMAN MEASLES STILL A THREAT

The nationwide effort to immunize young children against rubella (German measless) has been so successful that rubella appears to be vanishing as a childhood disease.
childhood disease.

But the immunization programs, which concentrate on preschool and young school-aged children, have not affected susceptibility to rubella among adolescents and young adults. According to articles in this week's **JAMA**, that can mean a problem for the segment of the population that is most vulnerable to the disease —unborn babies.

Although rubella is a mild infection in adults and children, the rubella virus can cause severe abnormalities in a developing fetus. Heart defects, deafness and cataracts are characteristics of congenital rubella syndrome, which also can include mental retardation and other organ system abnormalities.

In a **JAMA** editorial, Walter A. Orentein, MD, Medical Epidemiologist, and Wayne L. Greaves, MD, Epidemic Intelligence Service Officer, Centrs for Disease Control, Atlanta, write that rubella incidence among young school-aged children decreaed 89 percent between 1966-68 (prior to the approval of rubella vaccine and 1975-77. Incidence in 1980 declined 67 percent from 1979, and the first 35 weeks of 1981 showed a 46 percent reduction compared with the same period in 1980.

Among young adults, however, overall susceptibility rates remain at 10 to 20 percent, unchanged from the rate existing before the start of rubella vaccination programs in 1969, according to two other articles in the current **JAMA**.

Adolescents and young adults now account for a high proportion of all reported cases of rubella and have the greatest risk of disease. Before 1969, about 77 percent of cases occurred in children under 14 years of age. In 1979, 70 percent of cases occurred in persons older than 15 years.

Thus, susceptible women of childbearing age remain at high risk explaining why the incidence of reported congenital rubella syndrome has not decreased substantially in recent years. Between 1975 and 1979 (the last year for which final data are available), an average of 39 cases of the syndrome were reported annually, write Orenstein and Graves.

Vaccination programs proposed to protect this high risk group have been only partially successful, according to the editorial. Premarital screening does not reach women who become pregnant outside marriage, and prenatal screening is ineffective if hospitals do not follow up by vaccinating susceptible women after delivery.

Orenstein and Graves place much of the burden of further prevention of congenital rubella syndrome on physicians. They urge doctors to educate their patients about the dangers associated with rubella during pregnancy, about the need for vaccination and about the success of vaccination in preventing congenital rubella syndrome. They recommend vaccination for every patient whose blood test reveals a lack of antibodies against rubella.

In all 50 states, laws require vaccination against rubella for school entry. In 38 states, students at all grade levels are covered. But some states waive the requirement for adolescent women because of the fear that they might be pregnant at the time of vaccination and deliver babies with congenital rubella syndrome. These fears are not supported by the available data, say Orenstein and Graves.

The most aggressive, practical and ultimately successful approach to reducing the incidence of rubella, they suggest, would be comprehensive school laws requiring vaccination of all students from kindergarten through 12th grade.

To effect further reductions in the incidence of congenital rubella syndrome, mandatory requirements for rubella inmmunity should be considered for all institutions where adoelscents and young adults study and work, such as colleges, hospitals and many comercial firms. Orenstein and Graves point out that mandatory rubella vaccination in the military has essentially eliminated rubella in that community.

CLINICAL TRIALS OF AN ARTIFICIAL BLOOD TO BEGIN

It looks a little like runny mayonnaise, it is chemically related to teflon. And 16 years ago, in a vivid demonstration, it was shown that mice totally submerged in it could swim around happily and not drown.

The substance is known as artificial blood and the first commercially produced example —brand named Fluosol— is being readied for shipment to a network of medical centers for clinical trials, according to the medical news section of **JAMA**.

Fluosol, which is distributed in the U.S. by Alpha Therapeutics Corp., a subsidiary of the Green Cross Corp., of Osaka, Japan, has been approved for testing, but only in people who would otherwise refuse blood transfusions.

Most of these people will be members of Jehovah's Witnesses, a religious group that cites a biblical passage as grounds for refusing blood transfusions.

Two medical centers that have already received approval to begin using Fluosol are Michael Reese Hospitals in Chicago and Harbor/UCLA Medical Center in Los Angeles.

In Japan, where Fluosol has been used in some 500 patients, it appears that the compound may soon be approved by the Japanese equivalent of the FDA.

Flousol acts in the body as a medium for the transportation of oxygen, the same job that hemoglobin performs in real blood, However its effects last only about 72 hours and it lacks clotting factors and other properties of the real thing.

Certain physicians have expressed concern that wide-spread publicity about artificial blood might mislead potential blood donors into thinking they weren't needed.

On the contrary, blood donors are very much needed for the foreseeable future. Oxygen transporters such as Fluosol are not envisoned as a treatment of choice when blood is available, according to Alan Friedman, PhD, of Alpha Therapeutics.

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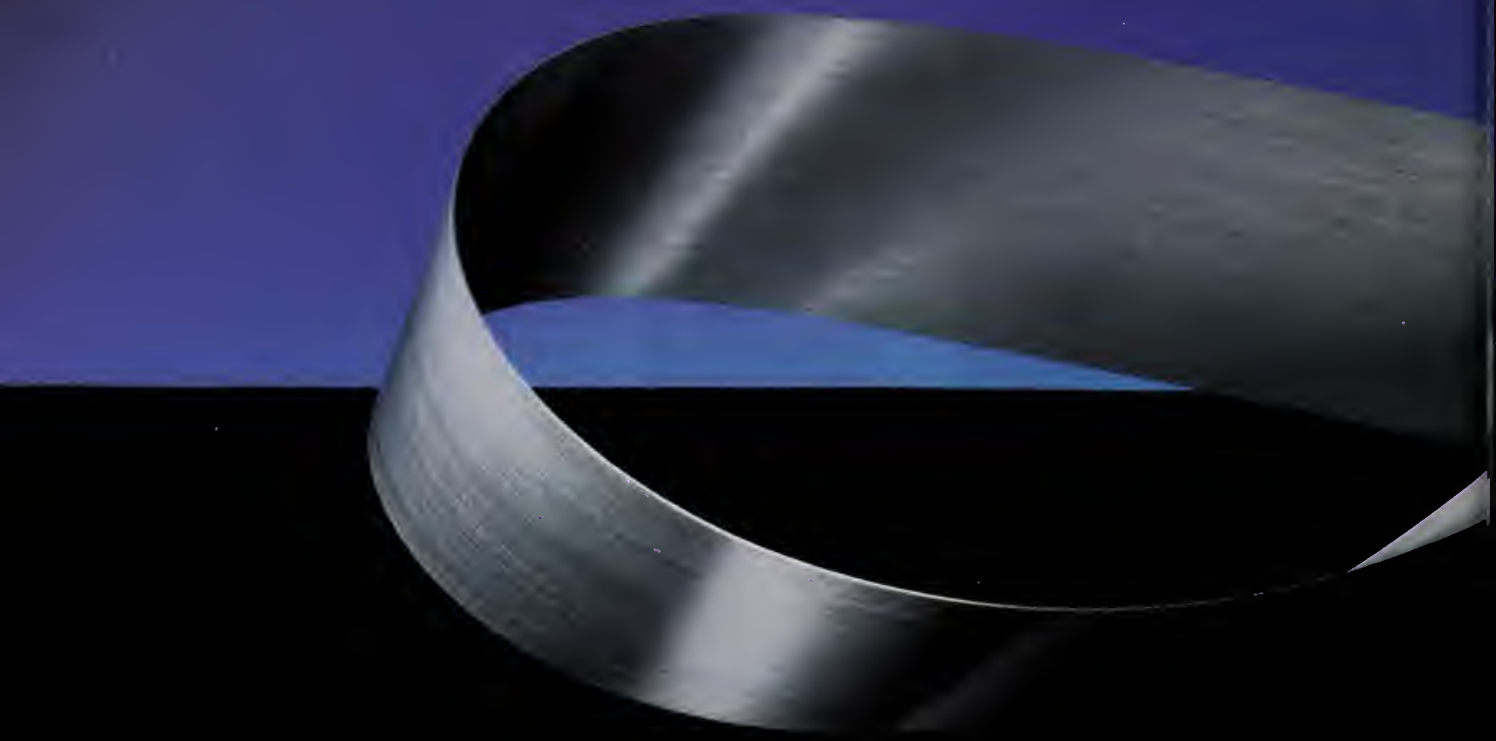

The Möbius Strip—a revolution in surface geometry

The Möbius Strip, discovered by August Möbius (1790-1868), is a unique geometrical figure. It is a two-dimensional object existing in three-dimensional space, having one plane surface and one edge, and forming a continuum which has intrigued generations of mathematicians and non-mathematicians alike.

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Indications: For relief of acute bronchial asthma and for reversible bronchospasm associated with chronic bronchitis and emphysema

Contraindications: In individuals who have shown hypersensitivity to any of its components.

Warnings: Status asthmaticus is a medical emergency. Optimal therapy frequently requires additional medication including corticosteroids when the patient is not rapidly responsive to bronchodilators

Excessive theophylline doses may be associated with toxicity and serum theophylline levels are recommended to assure maximal benefit without excessive risk. Incidence of toxicity increases at levels greater than 20 mcg/ml. Morphine, curare, and stilbamidine should be used with caution in patients with airflow obstruction since they stimulate histamine release and can induce asthmatic attacks. They may also suppress respiration leading to respiratory failure. Alternative drugs should be chosen whenever possible

There is an excellent correlation between high blood levels of theophylline resulting from conventional doses and associated clinical manifestations of toxicity in (1) patients with lowered body plasma clearances (due to transient cardiac decompensation), (2) patients with liver dysfunction or chronic obstructive lung disease, (3) patients who are older than 55 years of age, particularly males.

There are often no early signs of less serious theophylline toxicity such as nausea and restlessness, which may appear in up to 50 percent of patients prior to onset of convulsions. Ventricular arrhythmias or seizures may be the first signs of toxicity

Many patients who have higher theophylline serum levels exhibit a tachycardia.

Theophylline products may worsen pre-existing arrhythmias

Usage in Pregnancy: Safe use in pregnancy has not been established relative to possible adverse effects on fetal development, but neither have adverse effects on fetal development been established. This is unfortunately true for most antiasthmatic medications. Therefore, use of theophylline in pregnant women should be balanced against the risk of uncontrolled asthma

Precautions: Mean half-life in smokers is shorter than non-smokers; therefore smokers may require larger doses of theophylline. Theophylline should not be administered concurrently with other xanthine medications. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, liver disease, and in the elderly (especially males) and in neonates. Great caution should especially be used in giving theophylline to patients in congestive heart failure. Such patients have shown markedly prolonged theophylline blood level curves with theophylline persisting in serum for long periods following discontinuation of the drug

Use theophylline cautiously in patients with history of peptic ulcer

Theophylline may occasionally act as a local irritant to G.I. tract although gastrointestinal symptoms are more commonly central and associated with serum concentrations over 20 mcg/ml

Adverse Reactions: The most consistent adverse reactions are usually due to overdose and are

1. Gastrointestinal: nausea, vomiting, epigastric pain, hematemesis, diarrhea
2. Central nervous system: headache, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions
3. Cardiovascular: palpitation, tachycardia, extra systoles, flushing, hypotension, circulatory failure, life-threatening ventricular arrhythmias
4. Respiratory: tachypnea
5. Renal: albuminuria, increased excretion of renal tubular potentiation or diuresis, and red blood cells
6. Others: hyperglycemia and inappropriate ADH syndrome

Drug Interactions: Toxic synergism with ephedrine has been documented and may occur with some other sympathomimetic bronchodilators

Drug	Effect
Aminophylline with Lithium Carbonate	Increased excretion of Lithium Carbonate
Aminophylline with Propranolol	Antagonism of Propranolol effect
Theophylline with Furosemide	Increased diuresis of Furosemide
Theophylline with Hexamethonium	Decreased Hexamethonium-induced chromatropic effect
Theophylline with Reserpine	Reserpine-induced tachycardia
Theophylline with Chlordiazepoxide	Chlordiazepoxide-induced fatty acid mobilization
Theophylline with Cyclamycin (TAO=Triacetyloleandomycin), erythromycin, lincomycin	Increased Theophylline plasma levels

Caution: Federal law prohibits dispensing without prescription

For complete details, please see full prescribing information

Boehringer Ingelheim

Boehringer Ingelheim Ltd
Ridgefield, CT 06877

ASOCIACION MEDICA DE PUERTO RICO

BOLETIN

INSTRUCCIONES PARA LOS AUTORES

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia de contenido científico que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Se urge a los autores se esfuerzen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos no importa el tema o formato del manuscrito.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito

El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquinilla a doble espacio;por un solo lado de cada página, en TRIPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: Materiales y Métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

Nomenclatura

Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

Tablas

Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al meior entendimiento del manuscrito. Las tablas deben suplementar el texto, no duplicarlo.

Ilustraciones

Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arabigo), el autor, y debe indicarse la parte superior de la ilustración. Las leyendas de cada ilustración deben estar en hojas separadas.

Resumen

Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

Referencias

Las referencias deben ser numeradas sucesivamente de acuerdo a su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Deben utilizarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana. Las referencias deben seguir el patrón que se describe a continuación.

1. Para artículos de revistas: *Apellido(s) e iniciales del nombre del autor(es), título del artículo, nombre de la revista, ano, volumen, número, páginas. Por ejemplo:*
   Villavicencio R: Soplos Inocentes en Pediatría, Bol. Asoc. Med. PR 1981; 73 (10): 479-87
   Si hay más de 5 autores, incluir los primeros 3 y añadir et al.
2. Para citación de libros donde el autor(es) del capítulo citado es a su vez el (los) editor(es): *Apellido(s) e iniciales del autor(es), título del libro, número de edición, ciudad, casa editora, año y página, Por ejemplo:*
   Keith JD, Rowe RD, Vlad P: Heart Disease in Infancy and Childhood, 3d. Ed., New York, MacMillan, 1978, p. 789
3. Para citación de libros donde el editor(es) no es el autor(es) del capítulo citado se añade el autor(es) del capítulo y el título del mismo. Por ejemplo:
   Olley PM: Cardiac Arrythmias: In: Keith JD, Rowe RD, Vlad P Eds. Heart Disease in Infancy and Childhood. 3d Ed., New York, MacMIllan, 1978, p 275-301

Observar que no se usa el punto después de las iniciales de los autores ni al final de las referencias.

Cartas al Editor

Se publicarán a discreción de la Junta Editora. Deben estar escritas en maquinilla a doble espacio, no deben ser mayor de 500 palabras, ni incluir más de cinco referencias.

INSTRUCTIONS TO AUTHORS

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on scientific subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

All authors are urged to seek clarity, brevity, and pertinence in the manuscripts regardless of subject or format.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts

The entire manuscript, including legends and references should be typewritten double spaced in TRIPLICATE with ample margins. A separate title page should include the following: title, authors and their degrees (e.g. MD, FACP), city where the work was done, hospital or academic institutions, acknowledgement of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Case reports should follow the following order: Introduction, Materials & Method (if applicable), Summary of the case(s), Discussion, Abstract (English and Spanish), Acknowledgements, and References.

Nomenclature

Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurement should be used preferentially.

Tables

These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted. The language used in the tables must be the same as that of the article. Include only those tables which will enhance the understanding of the article. They should supplement, not duplicate the text.

Figures

Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

Summary

An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

References

These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text.

1. For periodicals: *Surname and initials of author(s), title of article, name of journal, year, volume, pages. For example:*
   Villavicencio R.: Soplos Inocentes en Pediatría. Bol Asoc Med PR 1981; 73 (10): 479-87
   If there are more than 5 authors list only 3 and add et al.
2. For books when the author o the cited chapter is at the same time the editor: *Surname and initials of author(s), title, edition, city, publishing house, year, and page. For example:*
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3. For chapter in book when the author of the chapter is not one of the editors:
   Olley PM: Cardiac Arrythmias. In: Keith JD, Rowe RD, Vlad P. Heart Disease in Infancy and Childhood, 3d Ed, New York, MacMillan, 1978, 275-301

Please note that the period is ommitted after the author's initials and at the end of the references.

Letters to the Editor

Will be published at the discretion of the Editorial Board. They should be typewritten double-spaced, should not exceed 500 words nor more than five references.

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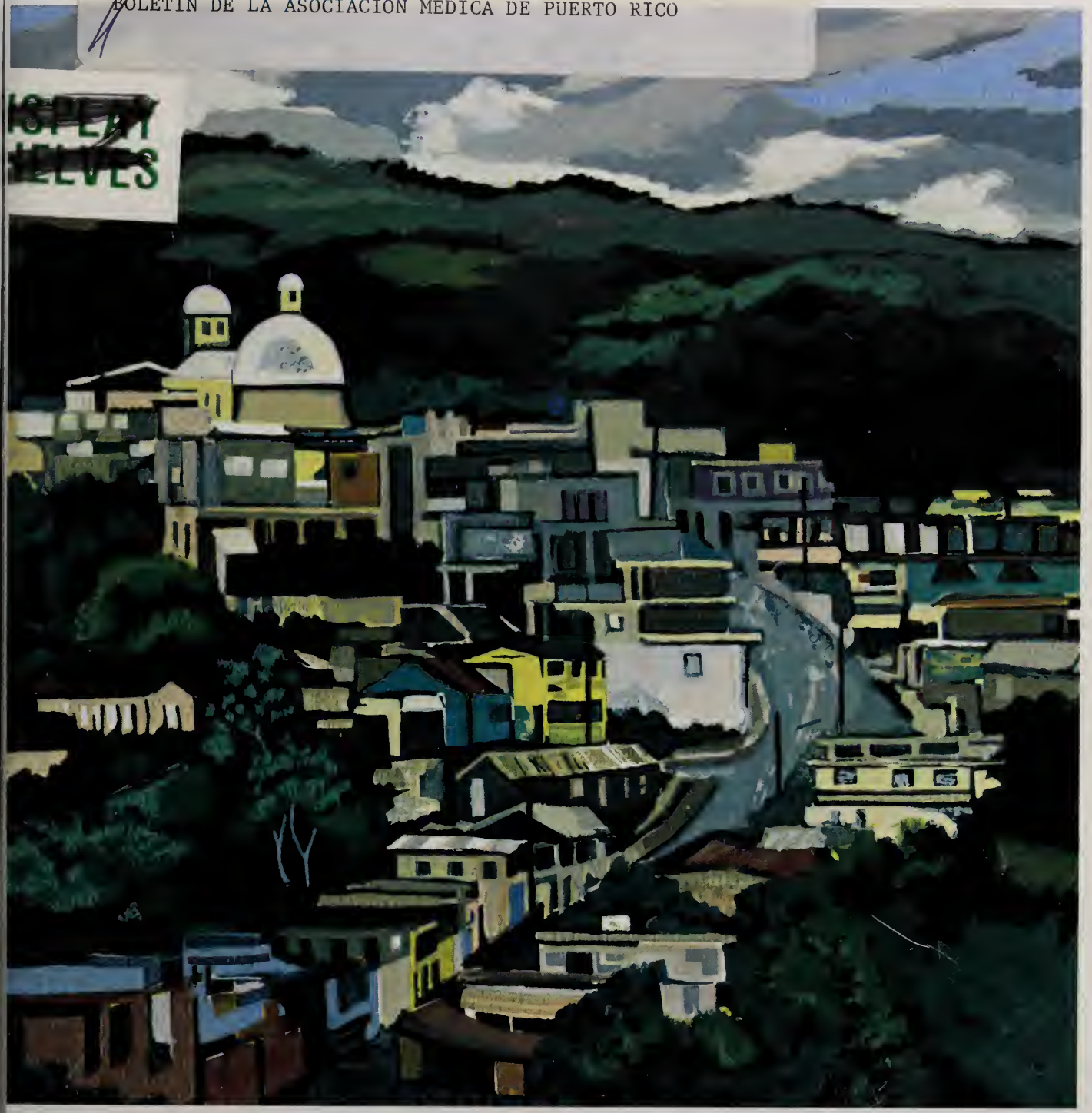
BOLETIN



VOL. 74/NUM. 3 MARZO 1982

For IPPB therapy and hand nebulizer

Alupent® Inhalant Solution

(metaproterenol sulfate) 5%

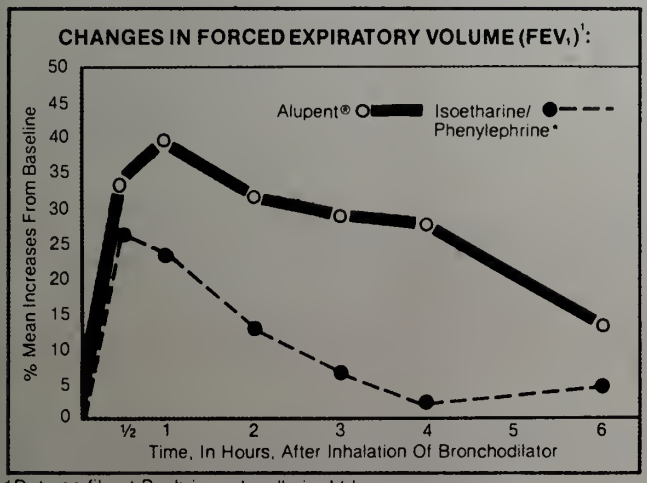
long needed...long lasting

A bronchodilator for relief of reversible bronchospasm associated with bronchitis, emphysema, and bronchial asthma.

- The Solution with a long duration of action

Up to 6 hours when administered by IPPB

- Prompt onset
- Effective for long-term use
- Adverse reactions similar to those of other sympathomimetic agents



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*This combination is no longer being manufactured in the United States. Isoetharine is now available as a single entity 1.0% solution.

How to use Alupent® Inhalant Solution (metaproterenol sulfate)

Method of Administration	Usual Single Dose	Frequency of Use	Range	Dilution
IPPB	0.3 ml	•For acute attacks—every 4 hrs. •For chronic bronchospastic pulmonary diseases-3 to 4 times a day.	0.2-0.3 ml	Diluted in approximately 2.5 ml of saline solution or other diluent
Hand Nebulizer	10 Inhalations	•For acute attacks—every 4 hrs. •For chronic bronchospastic pulmonary diseases-3 to 4 times a day.	5-15 inhalations	No Dilution

Please see brief summary on last page of this ad, for warnings, precautions and adverse reactions.

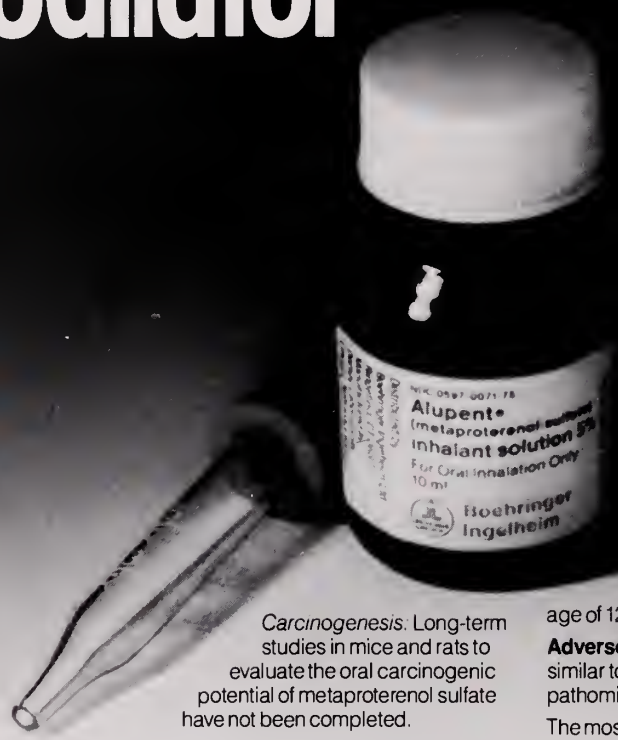
Alupent®

(metaproterenol sulfate)

Inhalant Solution

Bronchodilator

Alupent®
(metaproterenol sulfate)
Inhalant Solution
Bronchodilator



Alupent® (metaproterenol sulfate)
Inhalant Solution

Contraindications: Use in patients with cardiac arrhythmias associated with tachycardia is contraindicated.

Warnings: Excessive use of adrenergic aerosols is potentially dangerous. Fatalities have been reported following excessive use of Alupent, brand of metaproterenol sulfate, as with other sympathomimetic inhalation preparations, and the exact cause is unknown. Cardiac arrest was noted in several cases. Paradoxical bronchoconstriction with repeated excessive administration has been reported with sympathomimetic agents. Patients should be advised to contact their physician in the event that they do not respond to their usual dose of a sympathomimetic amine aerosol.

Precautions: Because Alupent, brand of metaproterenol sulfate, Inhalant Solution is a sympathomimetic drug, it should be used with great caution in patients with hypertension, coronary artery disease, congestive heart failure, hyperthyroidism or diabetes, or when there is sensitivity to sympathomimetic amines.

Information for Patients: Extreme care must be exercised with respect to the administration of additional sympathomimetic agents. A sufficient interval of time should elapse prior to administration of another sympathomimetic agent.

Carcinogenesis. Long-term studies in mice and rats to evaluate the oral carcinogenic potential of metaproterenol sulfate have not been completed.

Pregnancy: Teratogenic Effects: Pregnancy Category C. Alupent, brand of metaproterenol sulfate, has been shown to be teratogenic and embryocidal in rabbits when given orally in doses 620 times the human inhalation dose, the teratogenic effects included skeletal abnormalities and hydrocephalus with bone separation. Oral reproduction studies in mice, rats and rabbits showed no teratogenic or embryocidal effect at 50 mg/kg, or 310 times the human inhalation dose. There are no adequate and well-controlled studies in pregnant women. Alupent, brand of metaproterenol sulfate, Inhalant Solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Alupent, brand of metaproterenol sulfate, is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of Alupent Inhalant Solution in children below the age of 12 have not been established.

Adverse Reactions: Adverse reactions are similar to those noted with other sympathomimetic agents.

The most frequent adverse reactions to Alupent, brand of metaproterenol sulfate, are nervousness, tachycardia, tremor and nausea. Less frequent adverse reactions are hypertension, palpitations, vomiting and bad taste.

Overdosage: The symptoms of overdosage are those of excessive beta adrenergic stimulation listed under **Adverse Reactions.** These reactions usually do not require treatment other than reduction of dosage and/or frequency of administration.

How Supplied: Alupent, brand of metaproterenol sulfate, Inhalant Solution is supplied as a 5% solution in bottles of 10 ml with accompanying calibrated dropper. Store at room temperature, avoid excessive heat. Protect from light.

For complete details, please see full prescribing information.

Distributed by:
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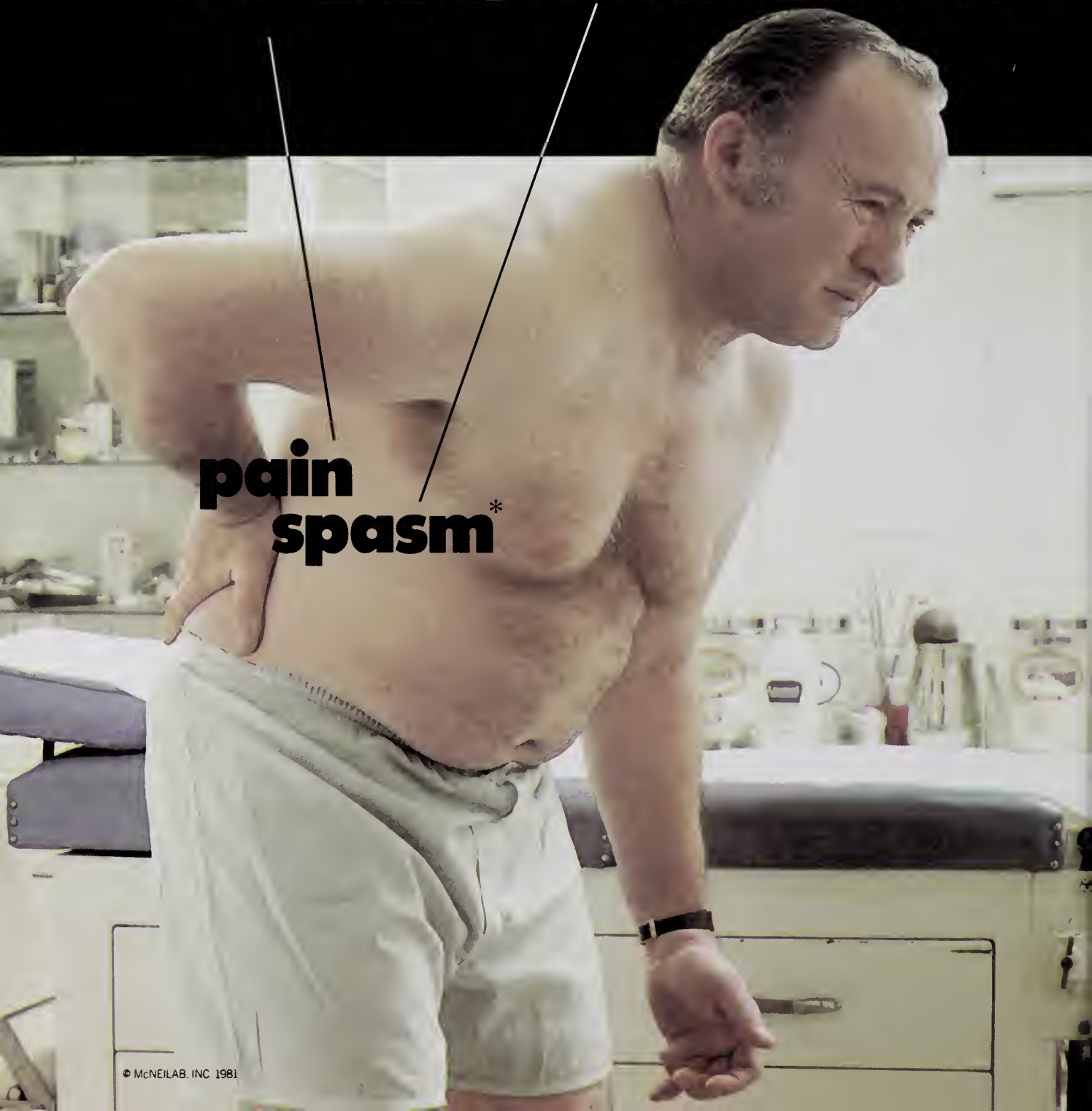
ASOCIACION MEDICA DE PUERTO RICO

BOLETIN

VOL. 74 - NUM. 3
MARZO 1982
ORGANO OFICIAL

DUAL PROBLEM



DUAL THERAPY

an analgesic + muscle spasm* relaxation

PARAFON FORTE provides the effective pain relief of TYLENOL® acetaminophen

PARAFON FORTE also provides the muscle spasm relaxation of chlorzoxazone.

PARAFON FORTE® tablets

(chlorzoxazone 250 mg plus acetaminophen 300 mg)

ummary of Prescribing Information

***Indications:** Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

"Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component

Warnings: Usage in Pregnancy—Use in women of childbearing potential only when potential benefits outweigh possible risks.

Precautions: Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or any signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped.

Adverse Reactions: Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While PARAFLEX® (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-seven patients, it was not possible to state that the dysfunction was or was not drug induced

Usual Adult Dosage: Two tablets q.i.d

Supplied: Light green tablets, imprinted "McNEIL" and "PARAFON FORTE"—bottles of 100 and 500. 18913

Caution: Federal law prohibits dispensing without prescription. Full directions for use should be read before administering or prescribing.

For information on symptoms/treatment of overdosage, see full prescribing information.

PARAFON FORTE tablets are manufactured by McNeil Pharmaceutical, Dorado, PR 00646

McNEIL PHARMACEUTICAL
McNEILAB, INC., Spring House, PA 19477

COLUMNA DEL EDITOR

Aparece en este número una nueva sección: *Medicina de Familia* la cual creemos será muy leída pues cumple con la mayoría de las peticiones de nuestros lectores: "publicación de temas prácticos y variados procurando que los mismos sean de interés general".

El Departamento de Medicina de Familia de la Escuela de Medicina de la Universidad de Puerto Rico comienza publicando dos artículos en la nueva sección. En uno de ellos, el Dr. Herman G. Stubbe, Director de dicho Departamento, revela los resultados de una encuesta sobre "¿Qué es el Médico de Familia?" En el artículo se define la misión de este especialista y se esboza el amplio espectro de la especialidad. En el segundo artículo de la sección se informa la experiencia clínica y epidemiológica de los autores durante un reciente brote de Dengue en la isla, aportando información nueva sobre esta enfermedad tropical.

La especialidad de Medicina de Familia está envuelta en la consecución del cuidado médico del paciente en su totalidad, pretendiendo evitar de esta forma la "fragmentación" de la medicina con respecto al paciente. En su práctica, los Médicos de Familia proveen una continuidad en el cuidado médico total del paciente, refiriéndolo a otros especialistas en caso necesario, pero manteniendo siempre un estrecho contacto con la totalidad de las necesidades de salud del enfermo. En la actualidad hay aproximadamente 7,500 residentes de Medicina de Familia en los Estados Unidos y Puerto Rico. Los nuestros comienzan hoy a publicar sus trabajos en el Boletín de la Asociación Médica de Puerto Rico, y este se encargará de proveerles la difusión nacional e internacional que ellos merecen por su esfuerzo y dedicación.

En este número también contamos con aportaciones de Radiólogos de nuestra comunidad médica. Uno de ellos ilustra con excelencia como se logra hacer el diagnóstico intrauterino de una malformación congénita por medio de la sonografía. La segunda contribución de estos especialistas aparece formando parte de la Sección de Autoevaluación donde el autor hace el diagnóstico mediante un estudio radiográfico que está al alcance de todos. Con la cooperación continuada de ellos confiamos hacer estas presentaciones sono-radiográficas de forma permanente, pues estamos convencidos tendrá una acogida favorable y será de gran provecho académico.

Estas innovaciones han sido posible gracias al nuevo enfoque, formato, y contenido que la Junta Editora ha estimado conveniente llevar a cabo en nuestra revista. Con ello persigue ampliar las fronteras para el intercambio de las experiencias científicas en el ámbito nacional e internacional, y que el órgano ofical de nuestra Asociación Médica sea el vehículo para su consecución. De esta forma se espera aumentar a su vez la calidad y utilidad de la revista.

Por ello exhorto a todos los compañeros médicos que dirijan sus experiencias médicas hacia el Boletín de la Asociación Médica de Puerto Rico. Con ello se evitará la "dilución" del esfuerzo y el trabajo científico que se lleva a cabo en nuestro país diariamente. Si el Boletín logra concentrar la comunicación de la experiencia médica del país, alcanzará para nosotros la más alta excelencia académica. El Departamento de Medicina de Familia de la Escuela de Medicina de la Universidad de Puerto Rico junto con dos Radiólogos en la práctica privada de su especialidad han dado el primer paso en esa dirección, esperamos que los demás le sigan.

Presidente Junta Editora
Boletín Asociación Médica de Puerto Rico

NUESTRA PORTADA:

"Lares", serigrafía por Isabel Bernal con fecha de 1981.

El pueblo de Lares está localizado en el centro de nuestra isla y corresponde orográficamente a la región denominada La Cordillera Central. Lares fue fundado en 1827 y se le llama "La Cuna de la Patria" por ser en este poblado donde el 23 de septiembre de 1868 tiene lugar la primera insurrección armada de separatistas puertorriqueños contra el Gobierno de la Corona Española.

El municipio de Lares limita por el oeste con San Sebastián, lugar de nacimiento de Isabel Bernal.

Relata la artista que motivada por los dibujos al carbón de su hermano mayor comienza a interesarse por la pintura desde su niñez. Al graduarse de Escuela Superior prosigue estudios en Mount Mary College en Milwakee, Wisconsin, donde aprende diseño y serigrafía sobre tela. Más tarde se traslada a la Universidad de Puerto Rico donde comienza a pintar con el Dr. Osiris Delgado y obtiene su Bachillerato en Artes.

Luego de graduarse comienza a trabajar en la División de Educación a la Comunidad del Departamento de Instrucción donde comparte labores con artistas de la talla de Lorenzo Homar, Rafael Tufiño, Epifanio Irizarry, Carlos Raquel Rivera, José Meléndez Contreras, y otros. Es observando a estos maestros de la pintura puertorriqueña, y trabajando junto a ellos que alcanza la culminación de su aprendizaje.

Sus pinturas y serigrafías han desfilado por las principales galerías de arte del país en múltiples exposiciones colectivas.

Nuestra artista pinta del natural y sus pinturas van desde el paisaje rural al urbano, y al retrato. Como puede apreciarse en la portada, Isabel capta magistralmente el ambiente puertorriqueño en una combinación armoniosa de colores que le prestan a sus cuadros un encanto nostálgico singular.

Isabel posee una vinculación familiar estrecha con la medicina puertorriqueña, pues su hermano mayor es el Dr. José Bernal Rosa, Cirujano. Además es prima-hermana de cuatro médicos: el Dr. Delfín Bernal Cabrero (Radiólogo), el Dr. Víctor Bernal del Río (Psiquiatra), el Dr. Bernal Vargas (Residente de Psiquiatría), y el Dr. Manuel Vargas Bernal, quien hace su Internado en el Centro Médico de Puerto Rico.

ALL FOR ONE ONE FOR ALL

Alexandre Dumas'
The Three Musketeers
and D'Artagnan

ONE FOR ALL – One tablet treats pinworm in any patient, regardless of age or body weight.* Obviates need to calculate individual dosages.

A single tablet eradicates pinworm in 95% of patients.

*Contraindicated in pregnant women and in persons who have shown hypersensitivity to the drug.

VERMOX® CHEWABLE TABLETS
(mebendazole)

JANSSEN PHARMACEUTICA

The #1 anthelmintic for pinworms and many other worm infestations

Please see complete Prescribing Information on adjacent page.

VERMOX® CHEWABLE TABLETS
(mebendazole)

Rx

Vermox
Tabs #4
Sig 1 tab
each family
member

DESCRIPTION VERMOX (mebendazole) is methyl 5-benzoylbenzimidazole-2-carbamate.

ACTIONS VERMOX exerts its anthelmintic effect by blocking glucose uptake by the susceptible helminths, thereby depleting the energy level until it becomes inadequate for survival. In man, approximately 2% of administered mebendazole is excreted in urine as unchanged drug or a primary metabolite. Following administration of 100 mg of mebendazole twice daily for three consecutive days, plasma levels of mebendazole and its primary metabolite, the 2-amine, never exceeded 0.03 μg/ml and 0.09 μg/ml, respectively.

INDICATIONS VERMOX is indicated for the treatment of *Trichuris trichiura* (whipworm), *Enterobius vermicularis* (pinworm), *Ascaris lumbricoides* (common roundworm), *Ancylostoma duodenale* (common hookworm), *Necator americanus* (American hookworm) in single or mixed infections. Efficacy varies as a function of such factors as pre-existing diarrhea and gastrointestinal transit time, degree of infection and helminth strains. Efficacy rates derived from various studies are shown in the table below:

	Whipworm	Common Roundworm	Hookworm	Pinworm
cure rates				
mean	68%	98%	96%	95%
(range)	(61-75%)	(91-100%)	–	(90-100%)
egg reduction				
mean	93%	99.7%	99.9%	–
(range)	(70-99%)	(99.5%-100%)	–	–

CONTRAINDICATIONS VERMOX is contraindicated in pregnant women (see Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

PRECAUTIONS *PREGNANCY:* VERMOX has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since VERMOX may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

PEDIATRIC USE: The drug has not been extensively studied in children under two years; therefore, in the treatment of children under two years the relative benefit/risk should be considered.

ADVERSE REACTIONS Transient symptoms of abdominal pain and diarrhea have occurred in cases of massive infection and expulsion of worms.

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US Patent 3,657,267
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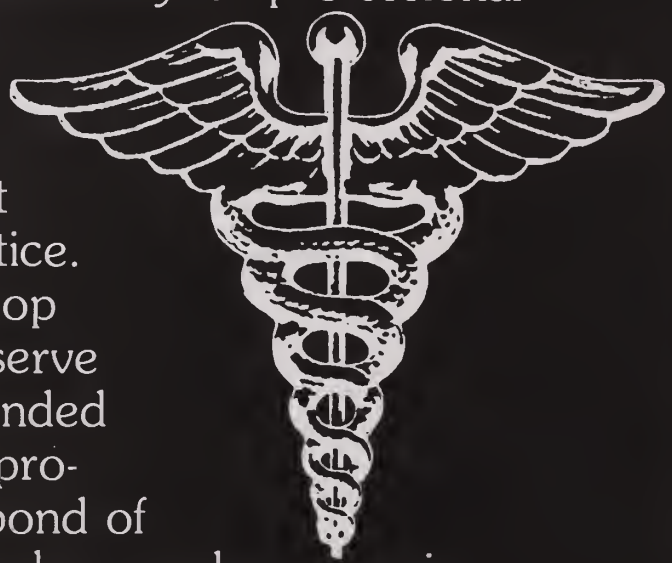

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CONTENIDO

EDITORIAL

Meningitis - 1982

La meningitis o inflamación de las meninges continúa siendo un problema clínico importante. Con los nuevos antibióticos la mortalidad se ha reducido en un 10-20%. En un artículo que aparece en esta revista la Dra. Muñoz presenta datos de 72 pacientes entre las edades de 30 días a 16 años admitidos con meningitis bacteriana al Departamento de Pediatría del Hospital Municipal de San Juan, el cual revela una tasa de mortalidad de 1%. La mayoría de estos pacientes tienen 6 años o menos.

El estudio revela que en los neonatos estudiados los bacilos gram-negativos entéricos fueron patógenos frecuentes. En tercer lugar *Streptococcus agalactiae* o los estreptococos del grupo B. Estos datos son similares a los que reporta la literatura en meningitis de neonatos.[1 7] Conociendo que la meningitis bacteriana es una emergencia médica y que el inicio de tratamiento debe ser empírico, el conocimiento de estos datos y de los de la literatura apuntan a que el tratamiento inicial empírico debe ser el uso de un aminoglucósido (amikacina, gentamicina o tobramicina) más ampicilina. La administración intraventricular de aminoglucósidos en este grupo es controversial, ya que se ha demostrado en un estudio una mortalidad más alta. Con la aparición en el mercado de las cefalosporinas de tercera generación como son cefotaxime, cefoperazone y moxalactam, el tratamiento inicial empírico puede ser que se cambie, sustituyendo una de éstas por el aminoglucósido. En el momento es necesario obtener datos experimentales sólidos sobre el beneficio de esto, antes de recomendar su uso.

Siendo en los niños entre las edades de 1 mes a 11 meses y de 1-6 años, el *Hemophilus influenzae* el microorganismo etiológico más frecuentemente reportado, debemos reconocer que desde el 1975 se han reportado casos en los E.E.U.U. de *H. influenzae* productores de beta-lactamasas resistentes a ampicilina.[2 5 7] En el estudio reportado en esta revista ninguna de las 44 cepas fueron resistentes a ampicilina. Durante el año 1981, el Laboratorio de Investigación en Enfermedades Infecciosas del Hospital de Veteranos, estudió un pequeño grupo de cepas de *H. influenzae* recobrados en el Centro Médico de Puerto Rico y encontramos una cepa productora de beta-lactamasa de un total de seis cepas estudiadas. El denominador no se tiene, ya que no todas las cepas recobradas fueron obtenidas para el estudio. Conociendo esto el tratamiento inicial empírico de meningitis bacteriana en niños debe ser el uso de ampicilina más cloranfenicol. Si *H. influenzae* es resistente a ampicilina debe utilizarse clorafenicol solamente y si fuese susceptible debe continuarse ampicilina solamente. En un futuro cercano podría recomendarse el uso inicial empírico de una cefalosporina de tercera generación como moxalactam más ampicilina, esperando los resultados de los cultivos.

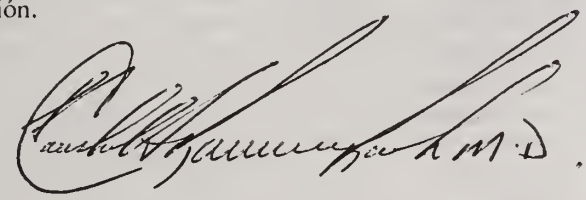
El manejo inicial empírico del adulto joven y el niño sobre 8 años con meningitis bacteriana requiere el uso de penicilina acuosa endovenosa. Los agentes etiológicos más frecuentes son *Neisseria meningitidis* y *Streptococcus pneumoniae*. Siendo en este grupo en donde ocurre con más frecuencia la meningitis meningococcica, es importante mencionar el uso de profilaxis. Profilaxis en casos de meningitis meningococcica documentada se limita a las personas que han tenido contacto íntimo con el caso índice. Contacto íntimo definido como transferencia de saliva, dormir en la misma habitación, resuscitación boca a boca, etc. Los agentes que se utilizan como profilaxis son rifampin o minociclina, ya que estos antibióticos penetran las secreciones paranasales y eliminan el estado de porteador.[1 7] También se ha recomendado profilaxis para los contactos de pacientes con meningitis por *H. influenzae* utilizando rifampin[8].

La meningitis bacteriana en el adulto es más frecuentemente causada por *Streptococcus pneumoniae* y requiere el uso endovenoso de penicilina acuosa. En los pacientes alérgicos a la penicilina con meningitis bacteriana el antibiótico de elección es cloranfenicol.

En el estudio reportado en la revista, no se encuentra diferencia en los parámetros del líquido cefaloraquídeo (LCR) entre los niños que no recibieron antibióticos y los que los recibieron antes de llegar al hospital. En un estudio realizado en adultos entre las edades de 12-19 años se demostró que los parámetros del líquido cefaloraquídeo cambiaron con pre-tratamiento dependiendo de la duración de este. Si el paciente había recibido antibióticos por 48 horas o más antes

de venir al hospital, los parámetros de glucosa, proteína y celularidad podían estar afectados y parecerce a aquellos observados en pacientes con meningitis no bacteriana.[9] Basándose en estos hallazgos, se estudiaron un grupo de pacientes prospectivamente utilizando los siguientes criterios para manejo: Todo paciente que recibió antibióticos por 48 horas o más antes de ser evaluado por su meningitis fue tratado como si tuviera meningitis bacteriana irrespectivo de los hallazgos en el LCR. Pacientes con pre-tratamiento por menos de 48 horas que tuvieron una tinción de grampositiva, o que no estuvieron alertas (evaluación clínica del médico) recibieron tratamiento como meningitis bacteriana irrespectivo de los hallazgos en el LCR. Los restantes (menos de 48 horas de pre-tratamiento y alertas) que tuvieron en el LCR una glucosa de menor o igual a 40 mg%, o una proteína mayor o igual a 150 mg/dl, o un contaje celular de 1,200 células blancas o más se trataron como meningitis bacteriana. Los restantes (el grupo mayor del estudio) fueron observados sin uso de antibióticos y el examen del LCR repetido en 8-12 horas.[10] Si el examen repetido del LCR llenaba uno de los criterios arriba expuestos se trataron como meningitis bacteriana. La mayor parte de los pacientes fueron dados de alta a sus casas en menos de una semana, y los costos y riesgos de hospitalización y antibióticos fueron reducidos.[10] Este esquema sólo aplica a personas entre las edades de 12-90 años, y no hay esquemas similares en pediatría.

La meningitis sigue con nosotros, el manejo de esta emergencia médica requiere un alto grado de sospecha, un análisis temprano del LCR y muchas veces repetirlo.[10] Requiere un conocimiento de los patógenos importantes en cada grupo de edad que guiará la selección del antibiótico o antibióticos a usarse inicialmente en base empírica.[12] No hay sustitutos para documentar la infección con cultivos. El trabajo de la Dra. Muñoz nos presenta la experiencia del Hospital Municipal en el manejo de meningitis bacteriana en 72 niños, estos datos pueden servirnos para el manejo de esta condición.



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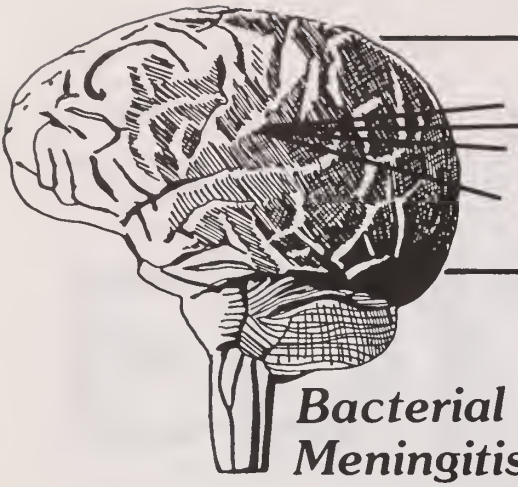

ESTUDIOS CLINICOS

Bacterial Meningitis in Pediatric Patients: A Five-Year Experience

Aurea I. Muñoz, MD

Abstract: Prospective data from 72 bacterial meningitis patients admitted at the San Juan City Hospital from October 1976 to April 1982 were reviewed. Pertinent clinical and laboratory features were examined, and the possible relevance of some of the findings as prognostic indicators was analyzed. Prolonged fever, late-onset or persistent convulsions, coma or semicoma on admission, and inappropriate ADH secretion, were associated with a high incidence of neurologic complications. Cerebrospinal fluid glucose content and Gram stain positivity were comparable in 32 patients with prior antibiotic therapy and in 40 untreated patients, but the mean cellularity and protein content were significantly higher in the latter group. The mortality rate was 1%.

Despite recent advances in therapeutics, central nervous system infections still cause significant morbidity and mortality in the pediatric age group. Periodic reappraisal of prevailing etiologic agents in different regions, and of significant clinical and laboratory features of such infections, is therefore warranted. The present report summarizes our experience with acute bacterial meningitis in pediatric patients over a five-year period.

Materials and Methods

The case records of all patients admitted to the pediatric ward of the San Juan City Hospital with bacterial meningitis were reviewed prospectively from October 1976 to April 1982. The etiologic diagnosis was based on recovery of the bacterial pathogen from cerebrospinal fluid and/or blood by routine culture methods. In the absence of reliable means for bacterial antigen detection in our midst during the study period, partially treated patients with negative cultures were excluded from analysis. Pertinent clinical and laboratory data were recorded on each patient, including the antibiotic treatment used, duration of fever, and complications. The case material includes patients ranging from 1 month to 16 years of age. There were 41 patients under one year of age, 29 in the 1-6 year age group, and 2 over 7 years old. Data from 15 patients under 4 weeks of age admitted during the study period were excluded from this report. There were 36 males and 36 females. Statistical analysis of the data was performed in consultation with the Department of Biomedical Statistics of the University of Puerto Rico School of Medicine.

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Results

Table I shows the distribution of causative organisms by age groups. Hemophilus influenzae was by far the most common pathogen (73%), followed by S. pneumoniae (9%). Group B streptococcus, enteric organisms, and S. epidermidis accounted for 3% of cases respectively. A 16 year-old boy with chronic renal failure, staphylococcal bacteremia and meningitis was the only death.

TABLE I

Organisms Causing Meningitis by Age Groups

	Age Group			
Microorganism	1-11mo	1-6yr	>7yr	Total
H. influenzae	29	24		53
S pneumoniae	3	3	1	7
Group B Strep.	3			3
S. aureus	1		1*	2
S epidermidis	2	1		3**
Enterics	3			3
N. meningitidis		1		1
Total	41	29	2	72

* A 16-year-old boy with chronic renal failure who was the only death.
** Two of these and the infant recorded under S. aureus were the only patients with ventricular system shunts in the series.

Additional Foci of Infection - Table II shows the number of patients in whom additional foci of infection were identified for each etiologic agent. Nearly one-half of patients had an identifiable focus elsewhere. The same organism was cultured from other secondary sites in only two instances, as follows: Staphylococcus aureus (soft tissue abscess), and S. epidermidis (infected surgical wound).

TABLE II
Patients with Additional Foci of Infection

Organism	Middle ear	Lungs	Skin & Soft Tissue
H. influenzae	12	13	2
S. pneumoniae	2	1	
Enterics		1	
S. aureus			1
S epidermidis	1		1*

* An 18 month-old girl with an infected ventriculoatrial shunt.

Clinical Laboratory Manifestations— All patients had fever (rectal temperature >37.7°C) during the course of their illness, although in one 35 day old infant the maximum temperature recorded was only 38°C. Vomiting, the next most common symptom, was present in 70% of patients. Convulsions, present in 23 patients, occurred before admission or early in the hospital course as a generalized seizure of relatively brief duration in 11 patients. More persistent or recurrent seizures, the majority of them with focalization, and usually starting after the third hospital day, occurred in 12 patients and will be hereinafter referred to as a seizure disorder. Eleven patients presented with coma or semicoma on admission.

The initial peripheral white blood cell count was elevated in the majority of patients. The mean value x 10^3 + 1 SD was 17.5 + 7.5/mm^3, with a range of 3.4 - 36.5 x 10^3. Otherwise unexplained anemia (Hb< 11 gm%) was identified in 54% of patients with H. influenzae meningitis and in 48% of the entire group. Serum Na determinations were done on 71 patients. Hyponatremia (Na <135 m eq/l) was present for varying periods of time in 19 patients who had vomiting, diarrhea or both, and in 16 patient without abnormal gastrointestinal losses who had evidence of inappropriate ADH secretion. (Criteria for this diagnosis were the presence of oliguria and a urinary specific gravity and/or osmolality higher than appropriate for a subnormal serum osmolality, in the absence of dehydration. The urine Na concentration was occasionally determined to confirm our impression). The blood culture was positive in 69% of patients with H. influenzae meningitis and in 62% of the entire group.

Cerobrospinal Fluid Findings - Table III relates the initial cerebrospinal fluid findings to prior antibiotic therapy. For the purpose of this analysis, we considered as partially treated those patients having received during their acute illness at least three oral doses of an absorbable antibiotic or one injection of a long-acting penicillin; the remaining patients in this category received at least two injections of a short-acting antimicrobial preparation. The mean values for cellularity, differential count, and protein content obtained in 40 patients with no preceding treatment were significantly higher ($p<0.05$) than those obtained in 32 partially treated patients (p for protein was >0.001). Mean glucose content and csf/blood glucose ratio, however, were comparable in both groups. The overall positivity rate of the Gram stain was 59% and that of spinal fluid culture 93% (in the five patients with a negative culture the organism was recovered from blood). Hemophilus influenzae was isolated from 26 of the 32 partially treated patients. Only one strain of H. influenzae, recovered from both blood and CSF of a patient pretreated with penicillin, was reported to be resistant to ampicillin. There were no chroramphenicol-resistant H. influenzae strains, and no penicillin - resistant pneumococci.

TABLE III
Comparison of Cerebrospinal Fluid Findings in Patient with Untreated and Pretreated Meningitis

Findings	Untreated (40 patients)	Pretreated (32 patients)	Significance (5% level)
Total WBC X10^3			
Mean ± 1 SD	3.0 ± 3.85	1.35 ± 1.44	S
Range	0.008 – 15.7	0.066 – 5.8	
% PMN			
Mean ± 1 SD	84.5 ± 15.7	73.0 ± 20.2	S
Range	42 – 100	16 – 100	
Glucose mg/dl			
Mean ± 1 SD	38 ± 25.5	39.8 ± 22.5	NS
Range	5 – 100	4 – 95	
CSF/Blood Glucose%			
Mean ± 1 SD	33.3 ± 22.6	31.4 ± 18.4	NS
Range	4 – 90	7 – 75	
Protein mg/dl			
Mean ± 1 SD	331.6 ± 284	157.9 ± 97.8	S*
Range	36 – 1240	26 – 416	
Culture +	37 (92.5%)	30 (93.7%)	
Gran Stain +	17/30 (56.6%)	13/21 (62.9%)	

* Significant at 0.1% level

Course and Complications - The temperature came down to normal (< 37.7°C rectally) after less than 72 hours of antibiotic treatment in 28% of patients, and within one week in 66%. Persistent or prolonged fever, defined in previous reports[1, 2] as one lasting for more than ten days after institution of appropriate antimicrobial therapy, was present in 10 patients (14%). Secondary fever, defined in the same reports as a rectal temperature > 38°C occuring after at least one afebrile day, was present in 9 patients (12%). Factors associated with secondary fever included an early change from the IV to the IM route of antibiotic administration (1 patient), intercurrent infection (2 patients), and drug hypersensitivity, possible cerebritis by scintigram, and ventriculitis in one patient each. There was no apparent cause for the fever in 3 patients. In no instance did a repeat lumbar puncture on a patient with persistent or secondary fever reveal bacteriologic relapse. As shown in Table IV, the proportion of seizure disorders and other neurologic abnormalities was higher in patients with persistent fever than in those with early defervescence or with secondary fever. Table V indicates the early neurologic complications in our patients. Subdural collections of fluid were demonstrated in 4 patients; three of the 4 had prolonged fever, and 2 had focal seizures. Purulent subdural fluid obtained from an infant with Proteus mirabilis meningitis yielded the same organism on culture. All effusions cleared within 1-3 weeks. Neurologic examination and a Denver developmental test performed at the time of discharge revealed residual abnormality in 10 patients (14%); four of these had hydrocephalus in addition.

TABLE IV

Neurologic Complications According to Fever Status

	No. of patients	Seizure disorder in hospital	Other complications
Fever <1 wk	48	5 (10%)	4 (8%)
Secondary fever	9	1 (11%)	1 (11%)
Persistent fever (>10 days)	10	6 (60%)	5 (50%)

TABLE V

Early Complications of Bacterial Meningitis

	Number of Patients	
Subdural effusion		4
Subdural empyema	1	
Neurologic deficit		10*
Motor impairment	4	
Developmental retardation	2	
Motor impairment and developmental retardation	3	
Ataxia	1	
Hydrocephalus		4**

* These include the four patients with hydrocephalus and two of the patients recorded under subdural effusion.

** These include two patients recorded under subdural effusion.

Discussion

The incidence of bacterial meningitis has increased over the past several decades, largely due to an increased frequency of meningitis due to H. influenzae, type b. Indeed, the great majority of cases (73%) in our patient population were due to H. influenzae, with Pneumococcus a distant second (9%). The finding of only 1 patient with Meningococcal meningitis is rather surprising; during the study period we had a few meningococcemia patients with negative CSF findings.

The age distribution of purulent meningitis has not changed significantly during the last 40 years; the infant 6 to 12 months of age is apparently at greatest risk, and 90% of reported cases occur between 1 month and 5 years of age.[3] The patients in our study sample, of whom 57% were from 1-12 months of age, conform to the expected age distribution for this disease.

Some investigators have found nomarked alterations in the cerebrospinal fluid findings at initial lumbar puncture as a result of prior antibiotic administration.[4] The data for glucose content and Gram stain positivity obtained in our untreated patients were comparable to those in the pretreated group, but the mean values for cellularity and protein content were significantly higher in the untreated patients. We have no explanation for this discrepancy.

The 62% incidence of positive blood cultures (69% in H. influenzae meningitis patients) underscores the fact that purulent meningitis usually follows hematogenous spread of bacteria from a distant focus of infection. In one study of H. influenzae meningitis, positive blood cultures were obtained from 82% of patients.[4]

Fever resolved within 72 hours in 28% of patients and within one week in 66%. Neither failure of defervescence within the first few days nor the advent of secondary fever after at least one afebrile day (12% of our patients) had any prognostic implications. Fever persisting beyond 10 days of adequate therapy (14% of patients) did seem to indicate a more severe disease process, since half the patients with this finding had significant neurologic complications. These observations are in accordance with some published reports,[2] as is the observed fact that neither persistent nor secondary fever was ever associated with failure to sterilize the CFS or with bacteriologic relapse.

Anemia, a frequent concomitant of severe infections, particularly those due to H. influenzae, has been considered by some authors as an unfavorable prognostic factor in meningitis.[6] Present in 48% of our patients, it had no predictive value regarding sequelae. Depressions in the initial white blood cell count have also been found to portend more severe disease.[4] It was not possible to ascertain this correlation in our study, since the WBC was less than 5 x $10^3/mm^3$ in only one patient.

Hyponatremia as a result of inappropriate ADH secretion has been found to correlate significantly with the development of neurologic sequelae.[4] In the present study, 6 of 16 patients with this finding had a seizure disorder during their hospital stay, and 6 had residual neurologic deficits at the time of discharge. Expressed differently, 6 of 10 patients with short-term neurologic sequelae had clinical and laboratory evidence of IADH secretion. As is the accepted practice in this disease, we enforced fluid restriction to 800-1000 cc/m^2 day (after correction of any existing deficits) until the urine output was

adequate and there were no laboratory parameters suggesting inappropriate secretion of ADH.

Seizures occur in about 30% of patients with bacterial meningitis (35% in our series) and are regarded by some investigators as a major predictor of neurologic deficit in this disease.[6] Others attribute prognostic significance only to seizures which are persistent, hard to control, or which have their onset late in the hospital course.[4] None of our 11 patients with brief, generalized seizures early in their illness had evidence of neurologic deficit. By contrast, 7 of 12 patients (58%) who had prolonged or recurrent seizures, usually with focalization and generally starting after the third hospital day, had early residual abnormalities; at least 1 of the 7 developed a chronic seizure disorder. This frequency of sequelae is significantly higher ($p < 0.001$) than that observed in the group of patients with no convulsions (6%).

All three patients with coma on admission and four of eight with semicoma had sequelae at the time of discharge. This significantly high incidence of abnormality ($p < 0.001$) related to a greatly impaired level of consciousness is in accord with prior observations.[6]

Subdural collections of fluid, a frequent concomitant of bacterial meningitis (up to 50% in some series),[7] might have been detected more often in our study had daily transillumination of the skull been done routinely on younger infants. Following current conservative trends in management, only the patient with subdural empyema and one patient with focal seizures had more than one subdural tap. All of the effusions cleared within one month.

In view of the ever-increasing emergence of ampicillin - resistant H. influenzae strains, it is worth noting that only one resistant isolate of this bacterium was recovered (from a patient admitted in 1976) from among the 53 subjects with H. influenzae meningitis. Indeed, 23 of these patients received only ampicillin, 200-400 mg/kg IV, for the duration of treatment. One of the twenty-three had persistent fever; none had neurologic sequelae or bacteriologic relapse. Three patients were treated with chloramphenicol alone (100 mg/kg) and had an uneventful course. The remaining patients received various combinations of both drugs. The decision to initiate therapy with chloramphenicol was frequently made if the patient was seriously ill on admission, or if fever did not subside within 72 hours of ampicillin treatment (after repeating a spinal tap which in all cases showed improved parameters and yielded sterile fluid). It is thus not surprising that patients with neurologic complications and most patients with persistent fever received chloramphenicol for variable periods of time. If the drug was initiated on admission it was often discontinued when sensitivity results were available. As previously indicated, no penicillin-resistant pneumococci were encountered.

The 14% incidence of neurologic abnormality at the time of discharge is comparatively low. In a prospective study of H. influenzae meningitis patients, Feigin and associates[4] found the corresponding figure to be 42%; evaluation of their patients included evoked response audiometry and detailed psychometric testing. They also noted a tendency for even major sequelae to disappear with time, so that neurologic including intelectual deficits were encountered in only 8% of patients at one year. The insufficient follow-up data available to us at this writing preclude an assessment of long-term sequelae in the study group; attempts to locate some patients lost to follow-up have been initiated. The mortality rate of 1% reflects the downward trend in the death rate from various infectious diseases, including bacterial meningitis, over the last several decades.

Resumen: **Se analizó prospectivamente la data de 72 pacientes con meningitis bacteriana admitidos al Hospital Municipal de San Juan de octubre 1976 a abril 1982. Se examinaron los hallazgos clínicos y de laboratorio pertinentes, así como la posible relevancia pronóstica de algunos de ellos. La frecuencia de tinciones de Gram positivas y el contenido de glucosa del líquido cefalorraquídeo fueron similares en 32 pacientes parcialmente tratados con antibióticos y en 40 pacientes no tratados; el contenido proteico y la celularidad fueron significativamente mayores en el último grupo. La tasa de mortalidad fue de 1%.**

Acknowledgement

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Hormonal and Testicular Volume Studies in Cryptorchidism

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Abstract: We studied testicular volumes and hormone levels in a group of 117 patients within six distinct diagnostic groups: unilateral cryptorchidism (50), bilateral cryptorchidism (15), orchiectomy for trauma or torsion (9), orchiectomy for cryptorchidism (15), unilateral agenesis (6) and normal individuals (22). For analytic purposes these were subdivided into homogenous age groups. Concerning testicular volumes, we found that the undescended testicle is smaller than normal, and that there is a hypertrophy of the normal testicle when the contralateral testis is undescended, congenitally absent or surgically removed. The sum of the total testicular volume is approximately the same in all groups except in bilateral cryptorchidism where there is a significant decrease in total testicular mass.

Testosterone levels are similar in all groups: however, there is a significant rise in leuteinizing hormone and follicle stimulating hormone levels in the bilateral cryptorchidism group.

This data are consistent with a model of the undescended testicle as a hyporesponsive end organ.

Cryptorchidism is a relatively common embryologically-determined disorder ocurring in 0.5 - 1% of male children. It's etiology remains unknown despite several elegant studies which have described the normal development and descent of the testis.[1,2]

In a group of children managed at our institution, we studied the presenting clinical picture, treatment and results of cryptorchidism. As an outgrowth of this, we subsequently studied in a group children recalled for examination of testicular volumes and hormonal levels in these patients with cryptorchidism.

MATERIALS AND METHODS

This report examines testicular volume and hormone levels in 86 children operated for cryptorchidism at the Puerto Rico Medical Center during the period of January 1965 to December 1978. In addition, nine patients with orchiectomy for trauma or torsion and 22 normal individuals were examined and tested. These were assigned to one of six study groups as follows: I. Unilateral cryptorchidism (50); II. Bilateral Cryptorchidism (15); III. Orchiectomy for trauma or torsion (9); IV. Orchiectomy for cryptorchidism (15); V. Unilateral agenesis (6); and VI. Normal testicles (22).

All patients were examined by the same investigator. Testicular length and width were measured with calipers. Testicular volume was calculated from the following formula: Volume = (length $-$ 1 mm) $\times$ (width $-$ 1 mm)^2 $\times$ (0.52). This has been shown to be a valid approximation of testicular volume by Laron and Zilka.[3]

Blood samples drawn between 9 A.M. and 12 noon were allowed to clot at room temperature and then centrifuged. The serum was stored at —20°C for future testosterone, using Radioimmuno assay kits (double antibody method) produced by Serono®. These determinations have been shown to be highly accurate and specific.[4]

The study groups were further divided into four groups by age at time of examination and testing: group A, 2-9 years (45); group B, 10-11 years (12); group C, 12-14 years (19); and group D, 15 years or older (41).

Testicular volumes, testosterone, luteinizing hormone and follicle stimulating hormone were determined for each group and the mean and standard deviation calculated. The means of the groups were compared using the Student's t-test for two universes, variances unknown. Significance was ascribed at a level of $P<0.05$. Those groups where less than four subjects were present were not considered for statitical analysis.

RESULTS

I. Testicular Volumes

The undescended testicle after orchidopexy in unilateral cryptorchidism was significantly smaller than its counterpart descended testicle in every age group, $P<0.05$ (Table I). In bilateral cryptorchidism, after orchidopexies, the right and left testicular volumes were similar in the age groups compared (Table II). In subjects over 15 years (group D), there appeared to be a compensatory hypertrophy by the normal testicle in cases where the contralateral testicle was abnormally small or absent (Table III). In patients with absence of one testicle (groups III, IV, V), there was a hypertrophic contralateral testicle. The degree of hypertrophy was less in group I with unilateral cryptorchidism after orchiopexy. The total testicular volume in all these groups (I, III, IV, V) appeared to be similar. Only in the group of bilateral cryptorchidism (II) was there a significantly smaller total testicular volume, ($P<0.05$).

TABLE I

Cryptorchidism Study
Testicular Volumes: Unilateral Cryptorchidism

Group	N	Undescended Testicle (cm^3)	Descended Testicle (cm^3)
A	23	0.25 ± 0.11	0.48 ± 0.20
B	7	1.06 ± 0.25	2.16 ± 1.17
C	11	1.43 ± 0.22	2.69 ± 1.13
D	9	4.12 ± 1.40	7.39 ± 1.06
Total	50	1.32	2.44

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TABLE II

Testicular Volumes: Bilateral Cryptorchidism

Group	N	Right (cm^3)	Left (cm^3)
A	8	0.37 ± 0.17	0.21 ± 0.08
B	1	0.67*	0.63*
C	0	—	—
D	5	2.73 ± 1.41	2.79 ± 0.98
Total	14	1.23	1.16

* Less than four subjects in group.

II. Hormonal Levels

A. Testosterone

There was no significant difference in serum testosterone levels in individuals over 15 years of age (group D) in any of the six study groups (Table IV). The same trend appeared to hold in the other age groups (A,B,C) although there were not enough subjects in each group to achieve statistical significance. Testosterone levels increased with increasing age, particularly during puberty, reaching a normal adult male range of 4-10 mg/ml by radio immuno assay.[4] All groups with subjects over 15 years fell within this range.

B. Luteinizing Hormone (L.H.)

There was a significant elevation of luteinizing hormone in the patients with bilateral cryptorchidism (group II) over 15 years of age ($P > 0.05$). The small numbers of subjects in the other age groups, did not allow for adequate comparison (Table V). Luteinizing hormone levels rose gradually with increasing age, reaching normal adult male levels of 5-20

TABLE IV

Testosterone Hormone Levels (ng/ml)

Study Groups	Age Groups (Years)			
	A (2-9)	B (10-11)	C (12-14)	D (15 Over)
I	0.98 ±0.43	0.95 ±0.44	3.76 ±2.64	6.56 ±1.86
II	0.81 ±0.31	0.88*	0.87*	6.94 ±3.70
III	—	—	15.17*	7.93 ±4.15
IV	0.88*	2.68*	1.95*	9.22 ±6.78
V	2.05 ±0.99	—	—	9.16*
VI	2.52 ±0.22	1.91*	2.76 ±0.99	6.84 ±2.18

— No data points

* Less than four subjects in group.

TABLE III

Testicular Volumes: Subjects Over 13 Years of Age

Group	Diagnosis	Undescended	Normal	Sum of Volumes
I	Unilateral Cryptorchdism	4.12 ± 1.40	7.39 ± 1.06	11.52
II	Bilateral Cryptorchidism	2.73 ± 1.41(R) 2.79 ± 0.98(L)	None	5.52**
III	Orchiectomy (Trauma, Torsion)	None	12.87 ± 3.37	12.87
IV	Orchiectomy Cryptorchidism)	None	11.97 ± 4.49	11.97
V	Unilateral Agenesis	None	16.17*	16.17*
VI	Normal	None	6.65 ± 1.47(R) 7.27 ± 1.85(L)	13.93

* Less than four subjects in group.

** Significantly smaller than other groups.

mIU/ml.[4] All but the bilaterally cryptorchid patients fell within this range.

TABLE V

L.H. Hormone Levels (mIU/ml)

Study Groups	Age Groups (Years)			
	A (2-9)	B (10-11)	C (12-14)	D (15 Over)
I	3.77 ±2.19	6.01 ±0.58	6.78 ±2.51	9.66 ±1.92
II	6.49 ±3.26	8.27*	—	39.94** ±3.62
III	—	—	7.45*	27.56 ±6.29
IV	5.96*	6.53*	8.29*	24.28 ±7.94
V	3.63 0.96	—	—	—
VI	4.82 ±0.68	4.92*	9.58 ±3.3	17.26 ±8.25

— No Data Points.
* Less than four subjects in group.
** *Significantly higher than all other groups (P>0.05).*

C. Follicle Stimulating Hormone (F.S.H.)

F.S.H. was elevated in those patients over 15 years of age with bilateral cryptorchidism (P>0.05) The small numbers of subjects in each of the younger subgroups prevent similar conclusions (Table VI). F.S.H. increased with advancing age particularly around the pubertal years. The normal adult male range by radioimmuno-assay is between 5-20 mIU/ml.[4] All groups with individuals older than 15 years fell within this range except for those with bilateral orchidopexies (group II).

DISCUSSION

This study confirms that the undescended testicle, after orchiopexy is smaller than the normal testicle, a finding amply documented in prior studies.[1 2 5] Less well documented is the compensatory hypertrophy of the contralateral descended testicle in unilateral cryptorchidism or of the remaining testicle in those cases where one of the testicle has been removed. This effect has previously been noted in both humans and animals, where the hypertrophied testicle allows for development of normal secondary sexual characteristics, linear growth and skeletal maturation.[3] The mechanism for this hypertrophic compensation is not clear. The present report indicates that the ultimate total testicular tissue is approximately the same in all groups studies, except for that which included bilateral cryptorchidism and orchidopexies.

TABLE VI

F.S.H. Hormone Levels (mIU/ml)

Study Groups	Age Groups (Years)			
	A (2-9)	B (10-11)	C (12-14)	D (15 Over)
I	3.88 ±1.33	4.93 ±1.94	7.45 ±2.92	11.88 ±4.36
II	3.62 ±1.17	0.95*	—	26.56** ±6.57
III	—	—	8.02*	17.42 ±6.77
IV	4.75*	7.39*	5.57*	19.87 ±6.14
V	5.61 ±2.02	—	—	20.57*
VI	—	—	—	—

— No Data Points.
* Less than four subjects in group.
** Significantly higher than all other groups (P <0.05).

Although the results of our testicular volume calculations in normals individuals are somewhat smaller than those reported in other series [3] this may be due to differences in measurement technique or to ethnic factors. The intergroup comparisons in our subjects, however, appear to be valid since a standard technique was utilized by the same investigator on a racially homogenous group.

The individuals with undescended testicle in these studies produced normal amounts of testosterone, as reported by other investigators.[1 5 6 7] Gonadotropin levels, however, were abnormal. Significantly elevated levels of leuteinizing hormone (L.H.) and follicle stimulating hormone (F.S.H.) were found in individuals 15 year or older with bilateral cryptorchidism. Whether this is due to the need for increased pretesticular stimulation for adecuate testosterone production or to failure of negative feedback by an abnormal seminiferous tubule is unknown. The finding of increased levels of L.H. and F.S.H. in our group of post-pubertal patients with bilateral cryptorchidism is in inconsistence with other studies that have noted no difference in gonadotropins in cryptorchid patients.[1] There is however evidence to support our findings. At one end of the spectrum, it is well documented that in cases of congenital or acquired absence of both testicles, there is a state of hypergonadotropism.[5 6 7 8] The difference between inhibition by testosterone or inhibin is not present in those cases with total testicular absence, whereas it appears to take place in bilateral cryptorchidism, at a higher gonadotropin level. This "altered thermostat" situation would be consistent with known feedback control mechanism by testosterone and inhibin on gonadotropins.[8 9 10 11 12 13] Testosterone produced mainly in the Leydig cells is a known potent inhibitor of L.H. secretion.[6 8 10 11] Inhibin is a proteinaceous material produced by the testis, probably in

the seminiferous tubules, which preferentially inhibits F.S.H. production but also has a less potent effect on L.H. levels.[12 13] In certain pathologic conditions where Leydig cells are normal but the germinal epithelium has been destroyed or damaged, L.H. levels remain in the normal range, but F.S.H. levels become abnormaly high, presumably due to insufficient inhibin action.[13] Other conditions where there may be damage to both Leydig cells and germinal epithelium, show high levels of both gonadotropins. Infertile oligospermic males of varied etiologies have been documented to have high levels of both L.H. and F.S.H.[14] Based on our results, the patients with bilateral cryptorchidism appear to fall within this broad group, with hypergonadotropism and relative infertility.

Resumen: Estudiamos los volúmenes testiculares y los niveles hormonales en un grupo de 117 pacientes con seis diagnósticos específicos: criptorquidismo unilateral (50), criptorquidismo (15), orquiectomía por trauma o torsión (9), agenesia testicular unilateral (6), y normales (22). Para propósitos de análisis, se dividieron estos pacientes en grupos etáreos homogéneos. Encontramos que el testículo no descendido es más pequeño que lo normal, y que ocurre una hipertrofia del testículo normal cuando el testículo contralateral no ha descendido, está congenitamente ausente o se ha extirpado quirúrgicamente. El total del volumen testicular es similar en todos los grupos, excepto en criptorquidismo bilateral, donde existe una disminución evidente en masa testicular.

Los niveles de testosterona son similares en todos los grupos. Sin embargo hay un aumento significativo en los niveles de hormonas foliculo estimulante y luteotrópica en el grupo de criptorquidismo bilateral.

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"Which of you is the one with the bubonic plague?"

Serial P Wave Changes in the Electrocardiogram of the Acute Myocardial Infarction

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Summary: **Abnormalities in the atrial complex were recorded in the ECG of 53% (101 patients) of 190 patients during the course of acute myocardial infarction. In sixty-four patients who showed serial P wave changes, only thirty-five have had clinical evidence of left ventricular failure. In fifty-seven patients who developed left ventricular failure, twenty-two showed no P wave changes in the ECG.**

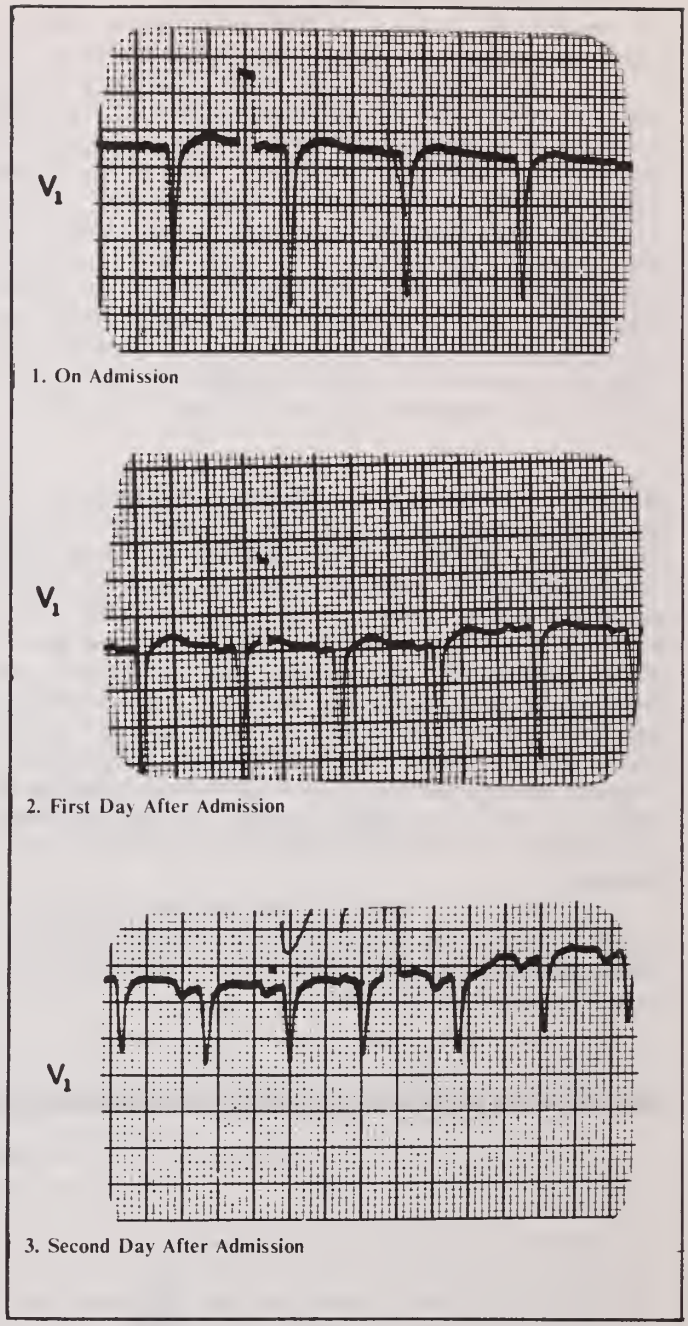
Serial P wave changes during acute myocardial infarction are not a valuable predictive tool for identifying patients who are at risk of developing left ventricular failure in the acute phase of myocardial infarction. Other electrocardiographic, echocardiografic or invasive methods should be considered for this purpose.

Ventricular failure within the course of myocardial infarction is an ominous sign[1] and establishing its relationship with thc electrocardiographic morphology of the P wave has been attempted [2-6]. The simplicity of this ECG variable, related to the left ventricular failure, can be put to clinical use, if proven useful.

In the present study, we reviewed the surface electrocardiogram (ECG) of patients with acute myocardial infarction, with special attention to the incidence of an abnormal atrial complex. Particularly, we studied the presence of serial P wave changes (Figure I) in predicting the development of left ventricular failure.

Material and Methods

Clinical and ECG records of 190 patients with acute myocardial infarction (AMI) admitted to the Mayagüez Medical Center during the years 1973 to 1976 were reviewed. The diagnosis of AMI was based on a positive clinical history associated with typical electrocardiographic changes and serum enzyme (SGOT and LDH) elevation. Left ventricular failure was diagnosed using the following criteria: a history of dyspnea associated with gallop rythm, crepitant lung rales, or typical chest roentgenologic changes[7] which were non-existent previously or which disappeared after treatment with diuretics, morphine, digitalis or vasodilators.



1. On Admission

2. First Day After Admission

3. Second Day After Admission

FIGURE 1

Before examining the electrocardiograhic data, we defined the following abnormalities in the atrial complex as significant:

Group I- P wave: When a P wave had a voltage greater than 0.25 millivolts or a duration longer than 0.12 seconds in lead II, and/or a negative component in V greater than 0.1 millivolt in amplitude or longer than 0.04 seconds[1] in duration. A P wave with an amplitude greater than 25% of the QRS complex was also considered within this first group.

Group II- PR segment: A segment depresed more than 0.8 mm or elevated more than 0.5 mm in any lead.

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Group III- Atrial Arrhythmias: Atrial flutter, atrial fibrillation premature atrial contractions and paroxysmal atrial tachycardia.

Group IV- Combined Atrial Complex Abnormalities: All the patients who showed more than one abnormality, such as mentioned above.

The serial P wave changes were obtained from the ECG's of patients with AMI while hospitalized and determined from the duration and amplitude of the terminal deflection of the P wave in leads II and V_1 in the manner described by Morris and associates.[8]

Variables were statisfically analized using the Chi-square test.

Results

The occurrence of atrial complex abnormalities (ACA) in the 190 patients with AMI was 53% (101 patients). The mortality rate of this group reached 30% (31 patients). This was similar to the patient without ACA (89 patients) in which 29% (26 patients) died.

P wave changes (group I) were the most frequently found abnormalities (Figuer II). They occured in 26% (49 patients) of the total population studied and in 48% of patients with ACA. The higher mortality rate was observed in the group of atrial arrhytmias (group III) in which 46% of patients died.

The incidence of complications associated with AMI was greater in the patients with ACA (64%) as compared with patients without ACA (49%). Left heart failure was more frequent in patients with ACA (40%) than in those without (19%).

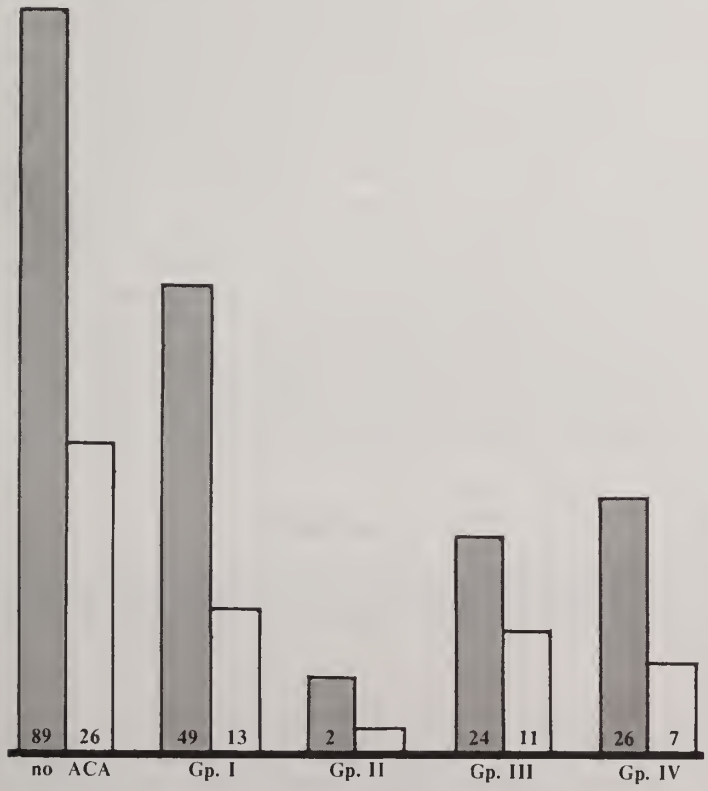

FIGURE 2
Incidence and mortality in the different groups.

Table I shows this relationship between the incidence of serial P wave changes and the presence or absence of left ventricular failure during the the episode of AMI. In the 57 patients with left ventricular failure, there were 22 patients who showed no ACA.

TABLE I

Relationship Between Heart Failure and Serial P Wave Changes

	Heart Failure	No Heart Failure	
Serial P wave Changes	35	29	64
No P Wave Changes	22	104	126
	57	133	

Sensitivity, specificity and predictive accuracy of serial P wave changes were determined as follows:

$$\text{Sensitivity} = \frac{35}{35 + 22} = 61\%$$

$$\text{Specificity} = \frac{104}{104 + 29} = 78\%$$

$$\text{Predicitive Accuracy} = \frac{35}{35 + 29} = 55\%$$

Discussion

We have observed that ACA's are a very frequent electrocardiographic finding in AMI. The electrocardiograhic parameters that we included in the study were easy to classify. A good reproductibility of these variables has been shown previously.[9]

The exact pathogenesis of an abnormal P wave during an AMI is not clear and it has been suspected to result from ischemic changes of the atrium, atrial overload with or without dilatation, and possibly from sympathetic over stimulation.

Previous reports have found P wave morhology to have some correlation with radiographically determined left atrial volume in valvular disease[10 11 12] in open heart surgery patients[13], and in arterial hypertension patients[14]. However, in patients with AMI the P wave duration or notched P wave in L_{II} was not related at all to left ventricular failure, but the terminal forces of the P wave in V_1 were closely associated with left ventricular failure[5]. We have found a greater incidence of left ventricular failure in patients with ACA as compared with patients without ACA, but it has no statistical significance ($P = 0.1$) Furthermore, the predictability of left ventricular failure with serial changes in the P wave morphology has been so poor that is not recommended as a clinically useful predictive sign, especially

if we consider the high incidence of this finding and the rate of false negatives in the population with AMI. The short-term mortality was not related in this series to a greater incidence of ACA or to serial P wave changes in the ECG's.

The presence of atrial complex abnormalities and serial P wave changes in the ECG of patients with AMI may well have more than one etiology. It may reflect variations in the anatomy, hemodynamics, or electrical physiology of the atrium. It's clinical use as a predictive sign should not be used for identifying who are at greater risk of developing left ventricular failure after an acute myocardial infarction. Other electrocardiographic variables, echocardiography or intravenous catheterization should be considered for this purpose.

Resumen

Los electrocardiogramas de 190 pacientes con infarto agudo de miocardio fueron revisados, encontrándose que 53% (101 pacientes) tenían anormalidades del complejo atrial. De 64 pacientes que mostraron cambios seriados en la onda P, sólo 35 manifestaron evidencia clínica de fallo ventricular izquierdo. De 57 pacientes que desarrollaron fallo ventricular izquierdo, 22 tenían ondas P normales en su ECG. Concluímos que los cambios seriados de la onda P durante infarto agudo de miocardio no tiene valor predictivo para identificar pacientes propensos a desarrollar fallo ventricular izquierdo durante la fase aguda del infarto y que otras variables electrocardiográficas, el ecocardiograma, y otros métodos invasivos deberían ser considerados para este propósito.

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MEDICINA DE FAMILIA

Herman G. Stubbe, MD

The Family Physician: A New Specialty

Many medical schools around the country established departments of family medicine during the last three years. By offering grants for funding these new departments, the U.S. Department of Health added a strong incentive for their establishment. In addition, medical schools had to have at least 50% of their graduates entering primary care graduate programs in order to receive capitation funds. Studies have shown that in medical schools with family medicine departments, more graduates enter family practice residencies, the bulk of primary care graduate programs.[1] Since the federal government is the single most important contributor to medical school funding[2] and many schools will have serious fiscal problems in the 1980's,[3] some medical schools may approve family medicine departments without a real understanding and commitment to family practice; therefore, it behooves the new family practice faculty to evaluate the existing faculty's understanding of and attitudes towards Family Practice.

There are valid reasons for this concern. First of all, because family medicine education is truly cross-disciplinary, it must have the cooperation of other specialties. Its goals and responsibilities, however, will differ from these specialties who may feel threatened by it, or may disagree and dismiss family medicine's basic concepts without considering them,[4] Secondly, the students' exposure to the other faculty's opinion of family practice may alter his/her view of the specialty.[5] Therefore, it is essential that every department of family medicine should try to teach the othr specialties the value and concepts of family medicine.

Methodology

At the University of Puerto Rico School of Medicine, the family medicine administrative unit was promoted from divisional to departmental status in August of 1979. A seven year old Family Practice Residency Program was already in existence. To evaluate the existing faculty's knowledge of, and attitudes towards Family Medicine, a questionnaire was mailed to all the fulltime faculty in September. The one page questionnaire entitled "THE ROLE OF FAMILY MEDICINE IN PUERTO RICO" was accompanied by a letter from the Department Chairman requesting the faculty person's help in defining this role. No information about Family Practice was provided.

The first question was designed to measure the faculty's estimated value of family practice by asking how much would a Residency-trained physician contribute to health care in (a) private practice; (b) public practice; (c) a Regional Hospital; (d) an Area Hospital; (e) a Community hospital; (f) primary care; (g) secondary care and, (h) tertiary care? To which the respondent would choose from the following answers: nothing, slightly, moderately, a lot, or greatly. In effect, the respondent had to make a judgement on the importance of a family physician in each of these health services.

A second question was designed to measure the faculty's attitudes towards the most conflictive issue in family practice: procedures. It read: do you think a Residency-trained family physician could do the following procedures without additional training? (a) vaginal deliveries; (b) C-sections; (c) minor surgery; (d) emergency surgery; and (e) endoscopies? The choice answers were yes, no, and I don't know. This was followed by the same question except for changing "without additional training" to "with additional training". The objective of this change was to differentiate negative attitudes towards family physicians doing procedures per se from an evaluation of residency training as insufficient training to perform these procedures.

Finally, an open-ended question asking for a detailed description of the family physician's functions was asked with the purpose of identifying the faculty's knowledge of Family Practice. To classify the results of this question, the following components of family practice were derived from the definitions given by the American Academy of Family Physicians (AAFP), the American Board of Family Practice (ABFP), and the American Medical Association (AMA), and from the written responses in the questionnaire: (a) primary care; (b) comprehensive care; (c) continuing care; (d) coordination of all of the patient's health care; (e) adequate referrals and consultations; (f) community involvement; (g) care for the entire family; (h) counseling; and (i) health promotion and education. Although some functions could be components of other functions, only specifically written responses are included in the results. For example, comprehensive care could be considered a component of primary care, but if the respondent did not specifically mention it, then it was not included in the results.

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Results and Discussion

The medical school faculty expects the new family physicians to make important contributions to health care delivery in both the private and public service with more expected in the public service (see Table I)

TABLE I

Family Physicians' contribution in Public and Private Practice

Practice	Greatly	A lot	Moderately	Slightly	Nothing
Private	40%	30%	18%	6%	6%
Public	53%	33%	12%	1%	0%

In Puerto Rico, the public health system is regionalized with primary care provided at Local Health Centers, secondary care at Area Hospitals, and tertiary care at the Regional Hospitals. The private sector is not organized, and general practitioners and non-primary care specialists provide primary care with the specialists usually providing the in-patient care. Since there is a very noticeable absence of qualified physicians at the local health centers, it is easier to identify the well-trained family physician's projected contribution there. Also the specialists' income would not be threatened in these centers as in private practice where those not trained to deliver primary care are providing it. In addition, results show that new family physicians are also expected to provide secondary care, and 17% even expected them to provide tertiary care (see Table II)

TABLE II

Family Physicians' contribution to Primary, Secondary, and Tertiary Care

Level of Care	Greatly	A lot	Moderately	Slightly	Nothing
Primary	73%	20%	6%	1%	0%
Secondary	20%	30%	28%	14%	9%
Tertiary	10%	7%	17%	35%	31%

This is probably the result of having seen our residents providing excellent care at the Regional Hospitals and in the medical centers. Therefore, it is not surprising to find that most specialists would try to circumscribe the practice of these new physicians to the primary care functions in the public health systems where they are most needed and less threatening.

Although only 17% think the family physician should provide tertiary care, 64% think that the family physician will contribute a lot or greatly to the care at Regional Hospitals (see Table III)

TABLE III

Family Physicians' Contribution in Hospitals

Hospital	Greatly	A lot	Moderately	Slighlty	Nothing
Regional	37%	27%	18%	15%	4%
Area	40%	35%	18%	5%	2%
Community	67%	27%	6%	3%	0%

This suggests that Regional Hospitals cannot be segregated solely by levels of care, and that consequently family physicians can effectively contribute to the care given there. The same suggestions can be made from the results on the Area Hospitals where 75% think they should provide secondary care.

Results of the question on procedures reveal that these new physicians are expected to be able to perform deliveries and minor surgery without additional training (see Table IV)

However, opinions are divided on C-sections even with additional training. These could reflect a lack of knowledge about the skills needed to permorm a C-section or an attitudional bias against family physician's encroachment on another specialty's field. Since the American College of Obstetrics and Gynecology has specified the additional training needed for family physicians to perform C-sections, one of the first activities of the new Family Medicine Department will be to publicize this accord.

Results on emergency surgery and endoscopies were similar in that both are expected to require more training than that given in a residency program. Because the question

TABLE IV

Faculty's view of Procedures Performed by Residency-trained Family Physicians

% of Faculty who:	Deliveries		C-Sections		Minor Surgery		Emergency Surgery		Endoscopies	
Approve	74%	95%*	10%	50%*	79%	94%*	54%	72%*	23%	63%*
Do not approve	20%	4%	79%	41%	13%	2%	26%	19%	51%	26%
Do not know	6%	1%	11%	9%	7%	4%	20%	9%	26%	11%

* With additional training

did not mention specific procedures under these categories, nothing further can be concluded except to note that in general there is less resistance to family physicians performing these procedures than C-sections; furthermore, the percent change of faculty approving of family physicians doing C-section *after* additional training is much higher that with other procedures suggesting that additional training is more important for performing C-sections than other procedures (see Table V)

TABLE V

Change in Faculty's view of performing procedures with additional training

% change of faculty who:	Deliveries	C-Section	Minor Surgery	Emergency Surgery	Endoscopies
Approve	28%	400%	19%	33%	174%
Do not approve	-80%	-48%	-85%	-27%	-174%
Do not know	-83%	-18%	-43%	-55%	-58%

Results of the open-ended question suggest either a lack of knowledge of family practice and/or a negative attitude towards the family physician's involvement in other than primary care (see Table VI)

TABLE VI

Open-Ended Question on Functions of the Family Physician

Function	% of Respondents identifying function
Primary Care (first contact)	55%
Adequate Referrals	35%
Care of Entire Family	29%
Comprehensive Health Care	28%
Community Involvement	15%
Counseling	11%
Continuing Health Care	8%
Coordinating all Health Care	8%
Patient Education	5%

Supporting the first interpretation is the lack of answers revealing essential components of family practice at the primary care level, such as patient education and counseling. As reinforcement of the latter suggestion is the fact that the second most common expected function of the family physician is adequate referrals.

Conclusions

Our survey demonstrates the need to educate our fellow physicians in other specialties on the definition of the new family physician. According to the Faculty of the Department of Family Medicine:

> "The essence of Family Practice lies in the comprehensive and continuing health care of patients in the context of their family and community. The Family Physician guarantees this health care by treating his patients as human beings, with dignity and respect, and by offering support and counseling. As head physician, he offers individualized care and guarantees the continuity of this care at all levels of medical practice, whether it be primary, secondary or tertiary. By educating his patients, he promotes health habits and maintains the health of his patients, thus improving the life styles of the families in the community where he lives and practices. He is an advocate for the patient within the system that affects his health and serves as coordinator of all the health services for the patient, his family and community. His genuine interest and involvement with his patients represents the moral and social commitment of the Family Physician."[6]

Thus, Family Physicians provide: primary care, comprehensive and continuing health care to the entire family; coordination of all of the family's health needs throughout all levels and all institutions or agencies of health care; counseling and patient education, and adequate referral when necessary. And, Family Physicians are involved in the community they serve because they are totally committed to the welfare of their patients.

Resumen: El Departamento de Medicina de Familia de la Escuela de Medicina de la Universidad de Puerto Rico se estableció en el 1979. Como primera actividad, hizo una encuesta de la facultad de la Escuela para medir el nivel de conocimientos y las actitudes hacia la medicina de familia. Los resultados demuestran la necesidad de informar a las otras especialidades sobre esta joven especialiad basada en el viejo concepto de que cada familia debe tener su médico de cabecera.

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A Clinical Survey of Reported Cases of Dengue-Like Illness During the Outbreak of Dengue 1981 in Puerto Rico

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Abstract: **Dengue, breakbone fever, an arthropod-borne tropical disease, is a viral condition which carries with it a high morbidity-mortality potential in the Caribbean population. There are four viral serotypes of dengue of which three have been recognized in Puerto Rico up to the current outbreak.**

During the dengue outbreak in Puerto Rico, comprising the months of September to December 1981, a total of 53 reported cases of dengue-like illness were clinically surveyed. The purpose of this study was to determine the most common clinical manifestations and incidence of serologically positive dengue. A surveillance program was established in four municipalities of the Caguas Health region. Patients were screened for dengue-like illness. A total of 53 paired blood samples were serologically tested for dengue. Only 9 (17%) of the cases were positive for dengue. The most common clinical symptoms were fever, myalgias, headache and retro-ocular pain present in 100% of the dengue positive patients. There were no significant hemorrhagic manifestations in the positive cases. Two cases were serologically positive for dengue 4, a serotype which had never been detected in Puerto Rico.

The low confirmation rate obtained and unspecificity of clinical symptoms found, confirms that dengue mimicks other viral diseases and that there are no clinical determinants which could differentiate between dengue serotypes.

Dengue fever, a viral disease transmitted principally by the Aedes aegypty mosquito, has been occuring in the Caribbean Region since the 19th century.[1] Dengue has been documented to have reached epidemic proportions in Puerto Rico during the rainy season periodically since the early nineteen hundreds.[2] The serotypes encountered have varied and include DN-1, DN-2 and DN-3.[3] The clinical manifestations are similar to other viral diseases; however, dengue carries with it a high morbidity-mortality potential which must be recognized in order to preclude Dengue Shock Syndrome and death.

This survey reports the clinical findings obtained during the outbreak of 1981 in the Caguas region. Peculiar to this outbreak is the recognition of DN-4 for the first time in Puerto Rico. Theoretically, the latter places the Puertorican population at a greater susceptibility since previous infections with the other three serotypes apparently does not confer heterotypic immunity.

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Material and Methods

A collaborative clinical study was established in the Caguas Health Region, an area located 10km south of San Juan, Puerto Rico. Family Physicians at the Health Centers of the initial visit and two weeks later paired samples were and at the family Practice Residency Program at the Caguas Regional Hospital, screened patients for dengue-like illness. This surveillance system was maintained during the 1981 outbreak of dengue, comprising the months of September through December. A dengue investigation sheet supplied by the San Juan Laboratories, Center for Disease Control, was filled for each patient. A complete physical exam and a standardized tourniquet test were performed. Platelet determinations were performed when the tourniquet test was positive.

Acute and convalescent blood samples were obtained on the initial visit and two weeks later paired samples were taken to the San Juan Laboratories where serological tests such as hemagglutination-inhibition, complement fixation, and virus isolation studies were performed to confirm dengue.

Dengue was confirmed when a 4-fold increase in hemagglutination-inhibition (HI) antibody was obtained between acute and convalescent samples. Primary dengue infection was defined as a rise antibody titer of no greater than 1:640 on the convalescent sample and an antibody titer of less than 1:10 in the acute sample. Patients with a convalescent serum sample titer of 1:1280 or greater, and an acute sample of 1:10 or greater were classified as having a secondary dengue infection.[4]

The severity of dengue was defined using a modification of the criteria outlined by the World Health Organization Technical Advisory Committee on Dengue Hemorrhagic Fever,[5] which is as follows:

Dengue Fever	Patients with only fever or fever with a positive tourniquet test with or without constitutional symptoms.
Grade II	Dengue fever with spontaneous hemorrhagic manifestations such as epistaxis or purpura.
Grade III	Narrowing of the pulse pressure to 20mm Hg or less, or hypotension in addition to the above symptoms.
Grade IV	Profound shock, no pulse or blood pressure detectable.

The tourniquet test was standardized. A sphygmomanometer was placed on the upper arm at 100mm Hg for 5 minutes. The appearance of 20 or more petechiae was considered a positive test.

Results

A total of 135 cases of dengue-like illness were surveyed. Paired samples were obtained for 53 (39%) of the cases out of which only 9 (17%) were positive for dengue. Hereafter, only

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CONTRAINDICATIONS: Not for use in the eyes or in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

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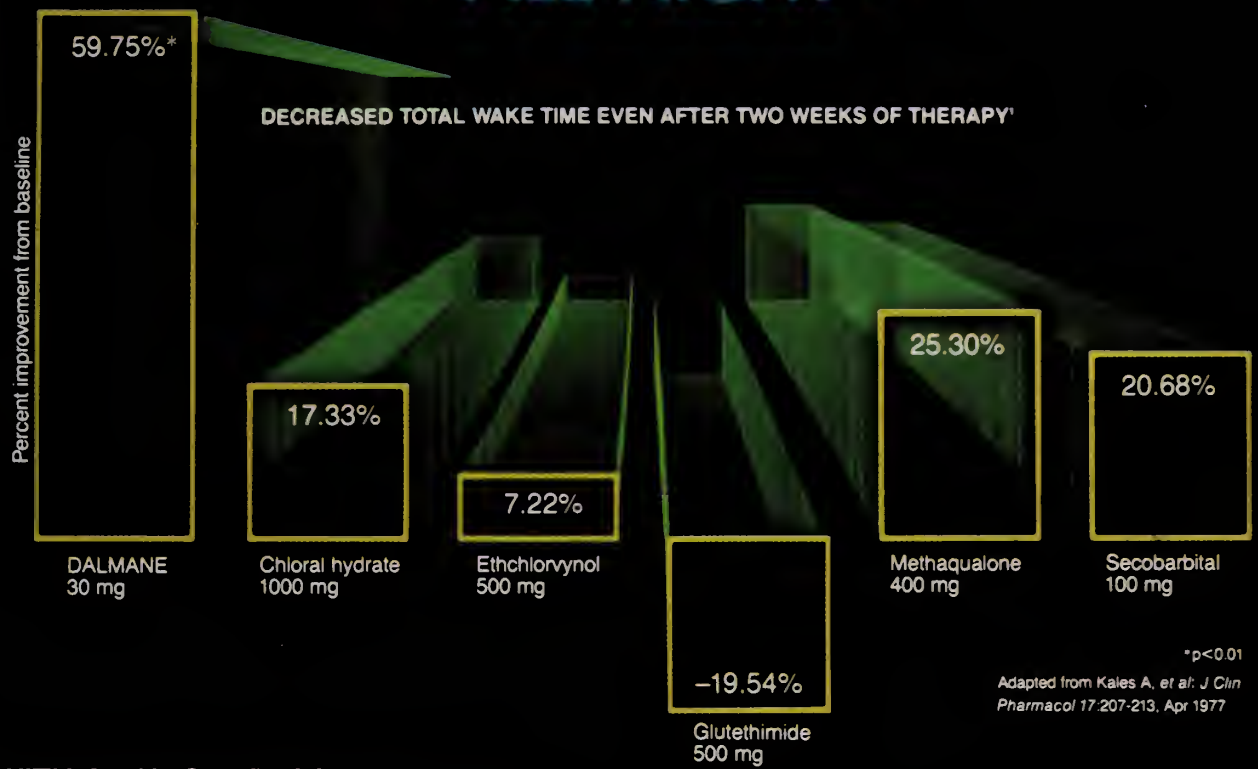

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Adapted from Kales A, *et al*: *J Clin Pharmacol* 17:207-213, Apr 1977

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–which have strong anticholinergic effects[10]

Antihistamines

–which are *not* reliable sleep-inducing agents[11]

–which may produce stimulation instead[11]

–which have anticholinergic effects[11]

Major tranquilizers

–whose side effects may be troublesome for nonpsychotic patients[12]

–where tolerance for sedation appears rapidly[12]

Dalmane does not cause significant worsening of sleep beyond baseline levels upon discontinuation.[4]

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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; in acute or chronic medical situations requiring restful sleep. Objective sleep laboratory data have shown effectiveness for at least 28 consecutive nights of administration. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended. Repeated therapy should only be undertaken with appropriate patient evaluation.

Contraindications: Known hypersensitivity to flurazepam HCl; pregnancy. Benzodiazepines may cause fetal damage when administered during pregnancy. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nighttime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity.

Dosage: Individualize for maximum beneficial effect.
Adults: 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients*: 15 mg recommended initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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Pfizer Laboratories Announces

THE FIRST ORAL CALCIUM CHANNEL BLOCKER FOR THE MANAGEMENT OF ANGINA PECTORIS

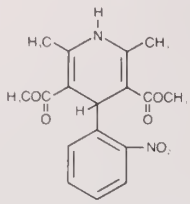
NEW PROCARDIA® (NIFEDIPINE) *Capsules 10 mg*

Please see PROCARDIA® *prescribing information on next page.*

PROCARDIA® CAPSULES
nifedipine

For Oral Use

DESCRIPTION: PROCARDIA (nifedipine) is an antianginal drug belonging to a new class of pharmacological agents, the calcium channel blockers. Nifedipine is 3,5-pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-, dimethyl ester, $C_{17}H_{18}N_2O_6$, and has the structural formula:



Nifedipine is a yellow crystalline substance, practically insoluble in water but soluble in ethanol. It has a molecular weight of 346.3. PROCARDIA CAPSULES are formulated as soft gelatin capsules for oral administration each containing 10 mg nifedipine.

CLINICAL PHARMACOLOGY: PROCARDIA (nifedipine) is a calcium ion influx inhibitor (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac muscle and smooth muscle. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels. PROCARDIA selectively inhibits calcium ion influx across the cell membrane of cardiac muscle and vascular smooth muscle without changing serum calcium concentrations.

Mechanism of Action: The precise means by which this inhibition relieves angina has not been fully determined, but includes at least the following two mechanisms:

1) Relaxation and prevention of coronary artery spasm: PROCARDIA dilates the main coronary arteries and coronary arterioles, both in normal and ischemic regions, and is a potent inhibitor of coronary artery spasm, whether spontaneous or ergonovine-induced. This property increases myocardial oxygen delivery in patients with coronary artery spasm, and is responsible for the effectiveness of PROCARDIA in vasospastic (Prinzmetal's or variant) angina. Whether this effect plays any role in classical angina is not clear, but studies of exercise tolerance have not shown an increase in the maximum exercise rate-pressure product, a widely accepted measure of oxygen utilization. This suggests that, in general, relief of spasm or dilation of coronary arteries is not an important factor in classical angina.

2) Reduction of oxygen utilization: PROCARDIA regularly reduces arterial pressure at rest and at a given level of exercise by dilating peripheral arterioles and reducing the total peripheral resistance (afterload) against which the heart works. This unloading of the heart reduces myocardial energy consumption and oxygen requirements and probably accounts for the effectiveness of PROCARDIA in chronic stable angina.

Pharmacokinetics and Metabolism: PROCARDIA is rapidly and fully absorbed after oral administration. The drug is detectable in serum 10 minutes after oral administration, and peak blood levels occur in approximately 30 minutes. It is highly bound by serum proteins. PROCARDIA is extensively converted to inactive metabolites and approximately 80% of PROCARDIA and metabolites are eliminated via the kidneys. The half-life of nifedipine in plasma is approximately two hours. There is no information on the effects of renal or hepatic impairment on excretion or metabolism of PROCARDIA.

Hemodynamics: Like other slow channel blockers, PROCARDIA exerts a negative inotropic effect on isolated myocardial tissue. This is rarely, if ever, seen in intact animals or man, probably because of reflex responses to its vasodilating effects. In man, PROCARDIA causes decreased peripheral vascular resistance and a fall in systolic and diastolic pressure, usually modest (5–10 mm Hg systolic), but sometimes larger. There is usually a small increase in heart rate, a reflex response to vasodilation. Measurements of cardiac function in patients with normal ventricular function have generally found a small increase in cardiac index without major effects on ejection fraction, left ventricular end diastolic pressure (LVEDP) or volume (LVEDV). In patients with impaired ventricular function, most acute studies have shown some increase in ejection fraction and reduction in left ventricular filling pressure.

Electrophysiologic Effects: Although, like other members of its class, PROCARDIA decreases sinoatrial node function and atrioventricular conduction in isolated myocardial preparations, such effects have not been seen in studies in intact animals or in man. In formal electrophysiologic studies, predominantly in patients with normal conduction systems, PROCARDIA has had no tendency to prolong atrioventricular conduction, prolong sinus node recovery time, or slow sinus rate.

INDICATIONS AND USAGE: I. Vasospastic Angina: PROCARDIA (nifedipine) is indicated for the management of vasospastic angina confirmed by any of the following criteria: 1) classical pattern of angina at rest accompanied by ST segment elevation, 2) angina or coronary artery spasm provoked by ergonovine, or 3) angiographically demonstrated coronary artery spasm. In those patients who have had angiography, the presence of significant fixed obstructive disease is not incompatible with the diagnosis of vasospastic angina, provided that the above criteria are satisfied. PROCARDIA may also be used where the clinical presentation suggests a possible vasospastic component but where vasospasm has not been confirmed, e.g., where pain has a variable threshold on exertion or in unstable angina where electrocardiographic findings are compatible with intermittent vasospasm, or when angina is refractory to nitrates and/or adequate doses of beta blockers.

II. Chronic Stable Angina (Classical Effort-Associated Angina): PROCARDIA is indicated for the management of chronic stable angina (effort-associated angina) without evidence of vasospasm in patients who remain symptomatic despite adequate doses of beta blockers and/or organic nitrates or who cannot tolerate those agents.

In chronic stable angina (effort-associated angina) PROCARDIA has been effective in controlled trials of up to eight weeks duration in reducing angina frequency and increasing exercise tolerance, but confirmation of sustained effectiveness and evaluation of long-term safety in these patients are incomplete.

Controlled studies in small numbers of patients suggest concomitant use of PROCARDIA and beta-blocking agents may be beneficial in patients with chronic stable angina, but available information is not sufficient to predict with confidence the effects of concurrent treatment, especially in patients with compromised left ventricular function or cardiac conduction abnormalities. When introducing such concomitant therapy, care must be taken to monitor blood pressure closely since severe hypotension can occur from the combined effects of the drugs. (See Warnings.)

CONTRAINDICATIONS: Known hypersensitivity reaction to PROCARDIA.

WARNINGS: Excessive Hypotension: Although in most patients, the hypotensive effect of PROCARDIA is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients on concomitant beta blockers.

Increased Angina/Beta Blocker Withdrawal: Occasional patients have developed well documented increased frequency, duration or severity of angina on starting PROCARDIA or at the time of dosage increases. The mechanism of this response is not established but could result from decreased coronary perfusion associated with decreased diastolic pressure with increased heart rate, or from increased demand resulting from increased heart rate alone.

Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of PROCARDIA treatment will not prevent this occurrence and might be expected to exacerbate it by provoking reflex catecholamine release. There have been occasional reports of increased angina in a setting of beta blocker withdrawal and PROCARDIA initiation. It is important to taper beta blockers if possible, rather than stopping them abruptly before beginning PROCARDIA.

Congestive Heart Failure: Rarely, patients usually receiving a beta blocker have developed heart failure after beginning PROCARDIA. Patients with tight aortic stenosis may be at greater risk for such an event, as the unloading effect of PROCARDIA would be expected to be of less benefit to these patients, owing to their fixed impedance to flow across the aortic valve.

PRECAUTIONS: General: Hypotension: Because PROCARDIA decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and titration of PROCARDIA is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure. See Warnings.

Peripheral edema: Mild to moderate peripheral edema, typically associated with arterial vasodilation and not due to left ventricular dysfunction, occurs in about one in ten patients treated with PROCARDIA. This edema occurs primarily in the lower extremities and usually responds to diuretic therapy. With patients whose angina is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction.

Drug interactions: Beta-adrenergic blocking agents: See Indications and Warnings. Experience in over 1400 patients in a non-comparative clinical trial has shown that concomitant administration of PROCARDIA and beta-blocking agents is usually well tolerated, but there have been occasional literature reports suggesting that the combination may increase the likelihood of congestive heart failure, severe hypotension or exacerbation of angina.

Long-acting nitrates: PROCARDIA may be safely co-administered with nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.

Carcinogenesis, mutagenesis, impairment of fertility: Nifedipine was administered orally to rats for two years and was not shown to be carcinogenic. When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose. *In vivo* mutagenicity studies were negative.

Pregnancy: Pregnancy category C. Nifedipine has been shown to be teratogenic in rats when given in doses 30 times the maximum recommended human dose. Nifedipine was embryotoxic (increased fetal resorptions, decreased fetal weight, increased stunted forms, increased fetal deaths, decreased neonatal survival) in rats, mice and rabbits at doses of from 3 to 10 times the maximum recommended human dose. In pregnant monkeys, doses 2/3 and twice the maximum recommended human dose resulted in small placentas and underdeveloped chorionic villi. In rats, doses three times the maximum human dose and higher caused prolongation of pregnancy. There are no adequate and well-controlled studies in pregnant women. PROCARDIA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

ADVERSE REACTIONS: In multiple-dose U.S. and foreign-controlled studies in which adverse reactions were reported spontaneously, adverse effects were frequent but generally not serious and rarely required discontinuation of therapy or dosage adjustment. Most were expected consequences of the vasodilator effects of PROCARDIA.

Adverse Effect	PROCARDIA (%) (N = 226)	Placebo (%) (N = 235)
Dizziness, light-headedness, giddiness	27	15
Flushing, heat sensation	25	8
Headache	23	20
Weakness	12	10
Nausea, heartburn	11	8
Muscle cramps, tremor	8	3
Peripheral edema	7	1
Nervousness, mood changes	7	4
Palpitation	7	5
Dyspnea, cough, wheezing	6	3
Nasal congestion, sore throat	6	8

There is also a large uncontrolled experience in over 2100 patients in the United States. Most of the patients had vasospastic or resistant angina pectoris, and about half had concomitant treatment with beta-adrenergic blocking agents. The most common adverse events were the same ones seen in the controlled trials, with dizziness or light-headedness, peripheral edema, nausea, weakness, headache and flushing each occurring in about 10% of patients, transient hypotension in about 5%, palpitation in about 2% and syncope in about 0.5%. Syncopal episodes did not recur with reduction in the dose of PROCARDIA or concomitant antianginal medication. Very rarely, introduction of PROCARDIA therapy was associated with an increase in anginal pain, possibly due to associated hypotension.

Several of these side effects appear to be dose related. Peripheral edema occurred in about one in 25 patients at doses less than 60 mg per day and in about one patient in eight at 120 mg per day or more. Transient hypotension, generally of mild to moderate severity and seldom requiring discontinuation of therapy, occurred in one of 50 patients at less than 60 mg per day and in one of 20 patients at 120 mg per day or more.

In addition, 2% or fewer of patients reported the following: **Respiratory:** Nasal and chest congestion, shortness of breath. **Gastrointestinal:** Diarrhea, constipation, cramps, flatulence. **Musculoskeletal:** Inflammation, joint stiffness, muscle cramps. **CNS:** Shakiness, nervousness, jitteriness, sleep disturbances, blurred vision, difficulties in balance. **Other:** Dermatitis, pruritus, urticaria, fever, sweating, chills, sexual difficulties.

In addition, more serious adverse events were observed, not readily distinguishable from the natural history of the disease in these patients. It remains possible, however, that some or many of these events were drug related. Myocardial infarction occurred in about 4% of patients and congestive heart failure or pulmonary edema in about 2%. Ventricular arrhythmias or conduction disturbances each occurred in fewer than 0.5% of patients.

In a subgroup of over 1000 patients receiving PROCARDIA with concomitant beta blocker therapy, the pattern and incidence of adverse experiences was not different from that of the entire group of PROCARDIA treated patients (see **Precautions**).

In a subgroup of patients with a diagnosis of congestive heart failure as well as angina, dizziness or light-headedness, peripheral edema, headache or flushing each occurred in one in eight patients. Hypotension occurred in about one in 20 patients. Syncope occurred in approximately one patient in 250. Myocardial infarction or symptoms of congestive heart failure each occurred in about one patient in 15. Atrial or ventricular dysrhythmias each occurred in about one patient in 150.

Laboratory tests: Rare, mild to moderate, transient elevations of enzymes such as alkaline phosphatase, CK, LDH, SGOT, and SGPT have been noted, and a single incident of significantly elevated transaminases and alkaline phosphatase was seen in a patient with a history of gall bladder disease after about eleven months of nifedipine therapy. The relationship to PROCARDIA therapy is uncertain. These laboratory abnormalities have already been associated with clinical symptoms. Cholestasis, possibly due to PROCARDIA therapy, has been reported twice in the extensive world literature.

OVERDOSAGE: Although there is no well documented experience with PROCARDIA overdosage, available data suggest that gross overdosage could result in excessive peripheral vasodilation with subsequent marked and probably prolonged systemic hypotension. Clinically significant hypotension due to PROCARDIA overdosage calls for active cardiovascular support including monitoring of cardiac and respiratory function, elevation of extremities, and attention to circulating fluid volume and urine output. A vasoconstrictor (such as norepinephrine) may be helpful in restoring vascular tone and blood pressure, provided that there is no contraindication to its use. Clearance of PROCARDIA would be expected to be prolonged in patients with impaired liver function. Since PROCARDIA is highly protein-bound, dialysis is not likely to be of benefit.

DOSAGE AND ADMINISTRATION: The dosage of PROCARDIA needed to suppress angina and that can be tolerated by the patient must be established by titration. Excessive doses can result in hypotension.

The starting dose is one 10 mg capsule, swallowed whole, 3 times/day. The usual effective dose range is 10–20 mg three times daily. Some patients, especially those with evidence of coronary artery spasm, respond only to higher doses, more frequent administration, or both. In such patients, doses of 20–30 mg three or four times daily may be effective. Doses above 120 mg daily are rarely necessary. More than 180 mg per day is not recommended.

In most cases, PROCARDIA titration should proceed over a 7–14 day period so that the physician can assess the response to each dose level and monitor the blood pressure before proceeding to higher doses.

If symptoms so warrant, titration may proceed more rapidly provided that the patient is assessed frequently. Based on the patient's physical activity level, attack frequency, and sublingual nitroglycerin consumption, the dose of PROCARDIA may be increased from 10 mg t.i.d. to 20 mg t.i.d. and then to 30 mg t.i.d. over a three-day period.

In hospitalized patients under close observation, the dose may be increased in 10 mg increments over four to six-hour periods as required to control pain and arrhythmias due to ischemia. A single dose should rarely exceed 30 mg.

No "rebound effect" has been observed upon discontinuation of PROCARDIA. However, if discontinuation of PROCARDIA is necessary, sound clinical practice suggests that the dosage should be decreased gradually with close physician supervision.

Co-Administration with Other Antianginal Drugs: Sublingual nitroglycerin may be taken as required for the control of acute manifestations of angina, particularly during PROCARDIA titration. See **Precautions, Drug Interactions** for information on co-administration of PROCARDIA with beta blockers or long-acting nitrates.

HOW SUPPLIED: Each orange, soft gelatin PROCARDIA Capsule contains 10 mg of nifedipine. PROCARDIA Capsules are supplied in amber glass bottles of 100 capsules (NDC 0069-2600-66).

The capsules should be protected from light and moisture and stored at controlled room temperature 59° to 77°F (15° to 25°C) in the manufacturer's original container.

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Pfizer LABORATORIES DIVISION
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the cases from which paired blood samples were obtained will be considered.

The total number of cases and the number of dengue positive patients for each municipality is given in Table 1. It is interesting to note that a significant number of positive cases came from San Lorenzo. Table 2 shows the distribution of reported cases and positive cases per month. Most cases were reported during the month of October; however, the confirmation rate remained stable throughout the months of September to November 1981.

TABLE I

Reported Cases and Confirmed Dengue Cases for Each Municipality

Municipality	Reported Cases	Percent	Confirmed Cases	Percent
Cidra	6	11.3	1	11.1
Caguas	15	28.3	1	11.1
San Lorenzo	17	32.1	5	55.6
Juncos	13	24.5	1	11.1
Other	2	3.8	1	11.1
Total	53	100.0	9	100.0

TABLE II

Distribution of Reported Cases and Confirmed Cases by Month

Month	Reported Cases	Percent	Confirmed Cases	Percent
September	8	15.1	3	33.3
October	34	64.2	3	33.3
November	10	18.9	2	22.3
December	1	1.9	1	11.1
TOTAL	53	100.0	9	100.0

The male to female ratio of the total cases was 1.0:1.5. This ratio changed to 1.0:1.2 when only confirmed cases were considered. The age distribution of reported cases and of confirmed cases of dengue is presented on Table 3. The median age was 25 years for both positive dengue and dengue-like illness. This finding closely agrees with the findings of the 1977 outbreak.[1] The severity of all nine dengue positive patients were all grade 1 or dengue fever. Seven cases were serologically identified as DN-1 and two cases as DN-4.

Table 4 shows the clinical manifestations observed in reported cases and in confirmed dengue cases. All dengue positive cases presented fever (100%) myalgias (100%), headache (100%), and retro-ocular pain (100%) as the most common clinical manifestations. These findings are not significantly different from dengue negative patients. Nevertheless, it is important to note that dengue negative patients had more frequent upper respiratory tract symptoms than dengue positive patients. The presence of a maculopapular rash was significantly greater in dengue positive patients. A biopsy performed to one of the patients

TABLE III

Age Distribution of Reported Cases and Dengue Cases

Age Group (Years)	Reported Cases	Percent	Confirmed Cases	Percent
0-4	0	0	0	0
5-9	3	5.7	1	11.1
10-14	9	17.0	1	11.1
15-19	8	15.1	0	0-
20-29	14	26.4	5	55.6
30-39	7	13.2	1	11.1
40-49	5	9.4	1	11.1
50-59	3	5.7	0	0
60+	4	7.5	0	0
TOTAL	53	100.0	9	100.0

with serologically proven DN-4, histologically revealed a perivascular monocytic infiltration without edema or vascular damage. These histologic findings have previously been reported in other dengue cases.[6]

TABLE IV

Clinical Manifestations Observed in Reported Cases and Confirmed Dengue Cases

Sign or Symptom	Dengue positive number	%	number	%
Fever	9/9	100.0	42/44	95.0
Myalgias	9/9	100.0	42/44	95.0
Headache	9/9	100.0	41/44	93.0
Retro-ocular pain	9/9	100.0	40/44	91.0
Arthralgias	8/9	89.0	33/44	75.0
Nausea/Vomits	8/9	89.0	29/44	66.0
Chills	7/9	77.0	41/44	93.0
Sore throat	5/9	56.0	30/44	68.0
Nasal congestion	4/9	44.0	26/44	59.0
Jaundice	4/9	44.0	2/44	4.5
Cough	3/9	33.0	32/44	73.0
Rash	3/9	33.0	8/44	18.0
Diarrhea	1/9	11.0	9/44	20.0

There were no significant hemorrhagic manifestations in any of the cases surveyed. The tourniquet test was performed on 40 patients and was positive in a total of 13 cases (32%) out of which only 2 (15%) were dengue positive. Platelet determinations were done on 12 of the patients with a positive tourniquet test, 11 of which had platelet counts over 100,000 per cubic millimeter. There were no other significant hemorrhagic manifestations observed in patients with a positive tourniquet test when compared to patients with a negative test. It is concluded that a positive tourniquet test is not a specific finding in dengue positive cases neither does it correlate with the platelet level.

Five of the nine confirmed cases of dengue had a primary antibody response and four had a secondary response. The severity of clinical symptoms was not different for patients exhibiting primary versus secondary dengue infection.

There were five patients hospitalized with dengue-like illness out of which only one was confirmed as dengue. Reasons for hospitalization were dehydration and thrombocytopenia. Two hospitalized patients died in whom Leptospirosis was subsequently confirmed.

Discussion

The low confirmation rate of 17% obtained through this survey, reaffirms the fact that Dengue Fever mimicks other viral diseases. It is also consistent with previous findings that the Caguas region is generally a low transmission area for dengue.[3] Presenting symptoms are nonspecific and there are no particular signs solely encountered in dengue. Viral diseases such as rubella, measles, influenza, viral exanthemas and other diseases such as leptospirosis and scarlet fever must be taken into consideration when dengue is being sought.[7] However, the presence of fever, myalgias, headache and retro-ocular pain highly suggest dengue. The presence of upper respiratory tract symptoms makes dengue unlikely.

Obtaining the convalescent serum sample has proven to be a difficult task; this was also true in our survey. Once symptoms have subsided and patients recover from their illness they are not motivated to return to the clinic to have their second sample drawn. Geographical isolation and lack of manpower makes it difficult to gather a greater percentage of paired samples. Nevertheless, the 39% reached in this study compares favorably with the aproximate 19% of paired samples received weekly at the San Juan Laboratories from the rest of the island at the peak of the dengue outbreak. We found that patient education about dengue and its complications contribute to a better response rate for convalescent samples.

In the Caribbean basin hemorrhagic manifestations secondary to dengue have not been a frequent finding during epidemics.[1] [2] This survey agrees with this previous observation. This evidence contrasts markedly with data reported from Southeast Asia where hemorrhagic and shock complications of dengue are a major health problem.[4] [9] [11] What apparently renders our population less susceptible needs to be studied.

An important observation to make is that there was no dengue-like illness reported for children ages 0-4 years. A similar finding was observed during the 1977 dengue epidemic.[1] Perhaps, it is frequently assumed that viral symptomatology during these ages has other etiologic agents but dengue. History taking and verbalization of complaints in this pediatric age group also contributes to the difficulty of suspecting dengue.

It is of particular interest that dengue 4 was serologically detected in one of the cases of our study in October 1981. This patient lives in San Juan and works in Caguas region. Subsequently, other dengue 4 cases have been serologically determined in other inhabitants of the area and virus isolation was possible in another of our cases evaluated in December 1981. One could speculate that the increase activity of this serotype in the Caguas region was imported from the San Juan Metropolitan area. There is an imperative need to recognize Dengue Hemorrhagic Fever and Dengue Shock Syndrome since the advent of a new serotype potentially heralds the beginning of a new outbreak or epidemic.

Resumen: El dengue es una enfermedad febril tropical de etiología viral transmitida por el mosquito Aedes aegypti. Hay varios serotipos virales del dengue de los cuales tres se han logrado identificar en el más reciente brote.

Durante el período comprendido entre los meses de septiembre a diciembre de 1981 se revisaron 53 casos reportados de enfermedad parecida al dengue. Se hizo el estudio para determinar las manifestaciones clínicas más frecuentes y la incidencia de dengue confirmado serológicamente. El programa abarcó cuatro municipios de la Región de Salud de Caguas.

Se tomaron 53 muestras de sangre de las cuales solo 9 (17%) fueron positivas para dengue. Los síntomas más comunes fueron: fiebre, mialgias, cefaleas y dolor retrocular los cuales estaban presentes en todos los casos en que hubo confirmación serológica de la enfermedad. No hubo manifestaciones hemorrágicas significativas en los casos positivos. En dos casos se identificó el serotipo dengue 4, el cual nunca se había detectado en Puerto Rico.

La tasa baja de confirmación obtenida y la inespecificidad de síntomas concuerda con el hecho de que el dengue simula otras infecciones virales y que no hay datos clínicos específicos que permitan diferenciar los diferentes serotipos del dengue.

Acknowledgments

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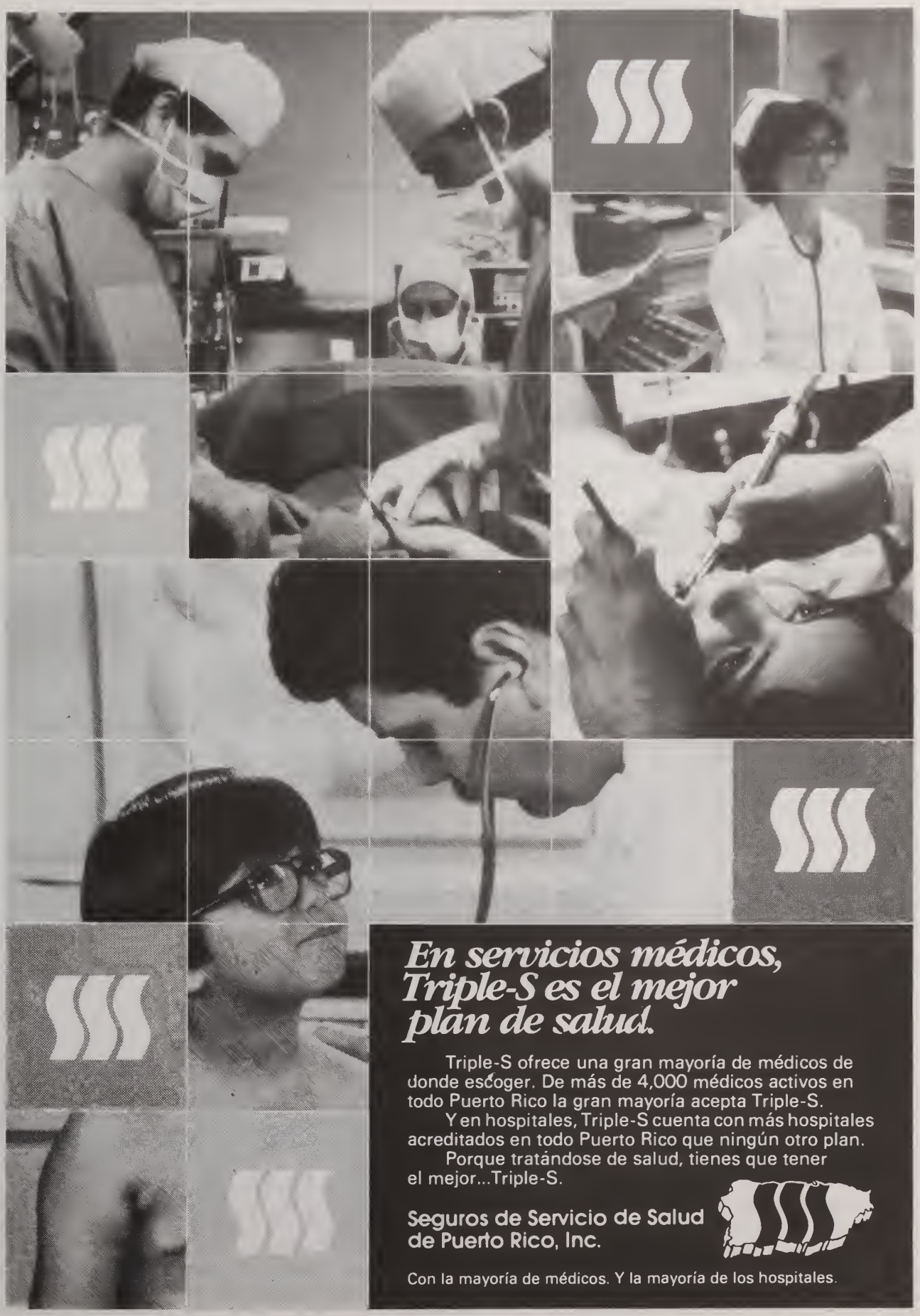

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PRESENTACION DE CASOS

Sonographic Demonstration of Congenital Duodenal Atresia in Utero

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Abstract: **Two cases of congenital duodenal atresia diagnosed in utero are presented. The typical sonograhic and radiographic findings as well as the differential diagnoses are discussed. The advantage of making the diagnosis prenatally in order to prevent possible perinatal complications is emphasized.**

With the improved resolution of the present ultrasound equipment gross congenital fetal anomalies are being frequently detected. This has prompted the routine use of sonography during the early second trimester by many obstetricians. Two cases in which the antenatal diagnosis of congenital duodenal atresia was made are presented.

Materials and Methods

The studies were performed using a comercially available digital static scanner and a 3.5 MHz transducer.

The system is also equiped with an integrated real time sector scanner which speeds the scanning process and is very useful in establishing fetal viability.

Clinical Observations

The two patients were multiparous women in the late third trimester of pregnancy. Both pregnancies were uneventful during the first and second trimesters.

The sonograms were requested in both cases because the uterus became too large for the menstrual dates during the third trimester. There were no associated signs of pre-eclampsia, vaginal bleeding or any other obstetric clinical abnormalities.

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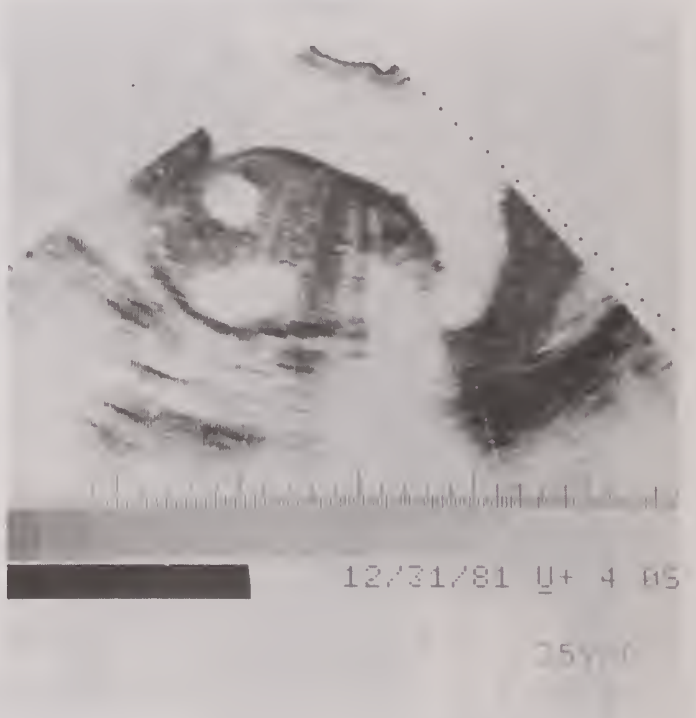
Discussion

Congenital atresia of the alimentary tract may occur anywhere between the pharynx and anus. Congenital doudenal atresia is an infrequent condition but is second only to ileal atresia as the most frequent cause of intestinal obstruction in newborns. It is presumed to result from a vascular accident during the recanalization process of the distal embryonic foregut[16].

Duodenal atresia is almost invariably associated with polyhydramnios.[1 2 3 4 5] Sonographically, two adjacent, cystic structures are identified in the anterior aspect of the fetal abdomen (Figs. 1A, 1B, 2A and 2B). These represent the dilated fluid-filled stomach and duodenal bulb proximal to the atretic duodenal segment.



Figs. 1A. Longitudinal sonographic section of the fetal abdomen.

After the fetus is born the upper alimentary tract is rapidly filled by ingested air producing the typical radiographic "double bubble" sign of duodenal atresia (Fig. 1C). The fetal abdomen is gasless beyond the obstructed segment. A word of caution in the antenatal diagnosis of intestinal atresia is presented by Skovbo, et. al,[8] where multiple fluid-filled bowel loops were identified in a normal fetus associated with idiopathic polyhydramnios. The fetus may swallow large amounts of fluid and present several filled

Fig. 1B Transverse sonographic section of the fetal abdomen.

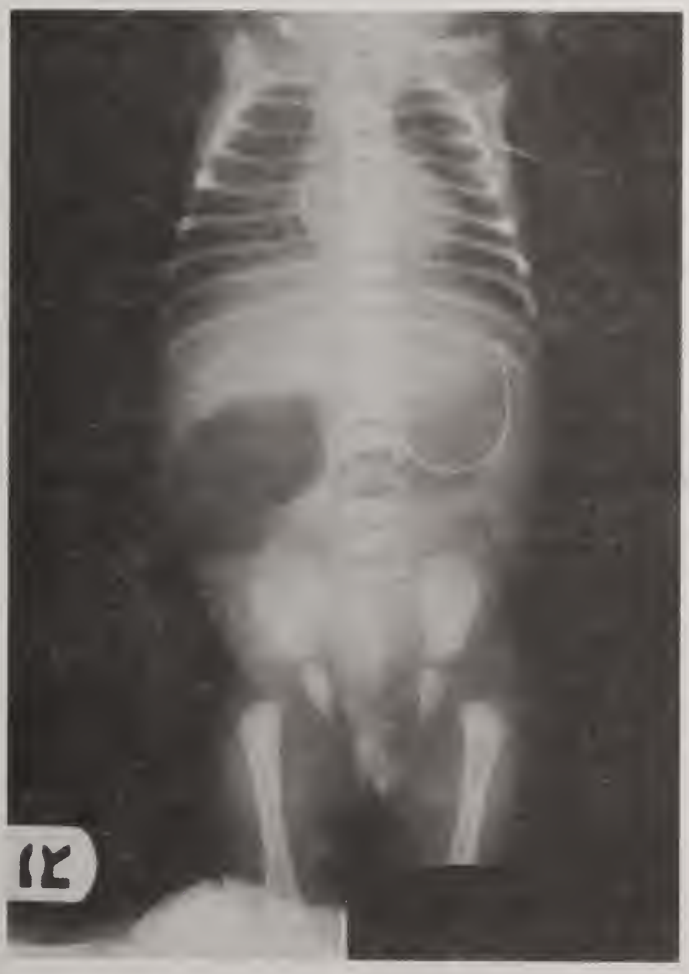


Fig. 1C. A KUB of the neonate showing the "double bubble" sign of duodenal atresia.

Fig. 2 A

Fig. 2 B

Figs. 2A and 2B: 2A) Longitudinal and 2B) transverse sonographic sections of another fetus presenting the signs of duodenal atresia.

bowel loops scattered throughout the abdomen. These findings should not be confused with intestinal atresia.

The differential diagnosis of abnormal intra abdominal fetal fluid collections include hydronephrosis, multicystic dysplastic kidneys, congenital intestinal atresia, ascites and ovarian cysts. All the above diagnostic possibilities may be associated with polyhydramnios.[1 9 13 15 18] Fetal renal abnormalities are not usually associated with excessive

amniotic fluid but polydydramnios has been recently reported in association with unilateral renal hydronephrosis[18] and unilateral multicystic dysplastic kidney[9].

The cause of the polyhydramnios is not clear. It may be a coincidental, idiopathic form of the condition or may result from extrinsic compression of the fetal G.I. tract by the cystic mass, thus preventing absorption of the ingested amniotic fluid.[9 15 18]

The most important aspect in the differential diagnosis is the relative intraabdominal location of the cystic mass. Multicystic kidney and hydronephrosis present as paraspinal retroperitoneal fluid collections. Differentiation between the two entities may sometimes be impossible antenatally but the pediatrician is alerted for prompt urologic work-up soon after delivery.

Fetal ascites and polyhydramnios are traditionally associated with Rh incompatibility but may occur in various non-inmunologic conditions[13]. The free intraperitoneal fluid surrounds the liver and outlines the falciform ligament. The fluid extends into the pelvic recesses and is readily differentiated from contained intraabdominal fluid collections. The affected fetus may also develop generalized anasarca evidenced sonographically by thick subcutaneous tissues.

Prenatal detection of cystic ovarian masses associated with polyhydramnios has been recently reported[15]. Although the cyst may be huge and extend into the fetal abdomen, they are usually pelvic in location and are easily differentiated from other higher abdominal or retroperitoneal fluid collections.

The antenatal diagnosis of duodenal atresia shold alert the pediatrician for prompt nasogastric suction soon after delivery in order to prevent aspiration pneumonia in the affected newborn. This is a very important aspect since the patient shold be in a stable condition for immediate surgical treatment.

The presented cases illustrate the value of routine obstetric ultrasonography in detecting congenital fetal anomalies. The importance of knowing the diagnosis before delivery cannot be overemphasized. The fetus should be delivered in an institution providing adequate nursing facilities and the neonatologist and pediatric surgeon should be alerted in order to minimize the potential perinatal morbidity and mortality.

Resumen: Se presentan dos casos de atresia duodenal congenita diagnosticados en utero. Se discuten los hallazgos sonográficos y radiográficos así como el diagnóstico diferencial. Se enfatiza la ventaja de conocer el diagnóstico prenatalmente para prevenir posibles complicaciones perinatales.

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ARTICULOS ESPECIALES

Determinación de Filiación y Paternidad

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Resumen: **La determinación de Filiación y Paternidad se ha visto favorecida en los últimos años por el desarrollo de nuevas técnicas inmunológicas y genéticas que permiten identificar individuos. Nuestros tribunales hacen amplio uso de las determinaciones de grupos sanguíneos, y HLA para decidir estos casos. Con las técnicas actuales en nuestras manos puede lograrse una probabilidad de exclusión o de inclusión por encima del 98%.**

Se resume aquí el fundamento de estas pruebas y su aplicabilidad.

El devenir del siglo XX con los descubrimientos de los grupos sanguíneos del sistema ABO por Landsteiner[1] en 1900 y por De Castello y Sturli[2] en 1901, junto con publicaciones posteriores[3 4 5] que indicaron su heredabilidad, permitieron el desarrollo de la inmunohematología y la inmunogenética, permitiendo en años subsiguientes transfusiones de sujetos, y transplantes de tejidos y órganos. En años posteriores fueron identificados otros grupos sanguíneos, pero el mayor estímulo a esta nueva ciencia provino del mismo Landsteiner quien junto con Wiener,[6] descubrió el factor Rh en 1940. Su hallazgo permitió una mayor aplicabilidad de las transfusiones sanguíneas y abrió nuevos enfoques en la eritroblastosis fetal.[7] Al presente son miles las publicaciones sobre los diversos grupos sanguíneos y sus aplicaciones, cumpliéndose la profecía de Landsteiner que los mismos serían algún día comparables a las huellas digitales de los individuos.

Su utilidad ha sido demostrada en múltiples procesos judiciales donde ha sido necesaria la identificación de sujetos utilizando grupos sanguíneos determinados en manchas y secreciones corpóreas,[8] al igual que para establecer la filiación de un sujeto. En casos de paternidad disputada y filiación, muchos estados exigen su determinación, como hemos logrado en nuestro país estableciendo jurisprudencia al respecto[9] para poder decidir un caso.

Al presente existen más de 20 sistemas de grupos sanguíneos, proteínas y enzimas que permiten incluir o excluir individuos con una probabilidad por encima del 99%. El grado de exclusión-inclusión dependerá del número de pruebas realizadas y de la incidencia de estos factores en la población normal (Tabla 1). Wiener[10] derivó una fórmula que permite determinar la probabilidad de exclusión, y por ende de inclusión, a partir de la frecuencia en la población normal de los factores analizados: $P= 1-(1-P_1)(P-P_2)(1-P_3)$ etc, donde P es igual al grado de exclusión en cada sistema. Por ello, la probabilidad de exclusión utilizando los sistemas ABO, MNS, Rh-Hr es de 61.4%, con todos los grupos anotados en la Tabla I es de 99.99%. Esta cifra implica que el 99.99% de los hombres falsamente acusados serían excluidos o el sujeto acusado tendría un 99.99% de inclusión de no probarse incompatibilidad. Este último dato constituye una cifra estadística irrefutable en cuanto a probabilidad en una corte. Si tenemos en cuenta que múltiples leyes científicas se establecen con 95% de probabilidad, este valor es lógicamente significativo.

Todos estos estudios pueden servir de base para identificación personal, diferenciar gemelos idénticos de dos fraternales, determinar relaciones filiales de padres a hijos, en niños confundidos en guarderías infantiles, niños secuestrados, filiación de paternidad en casos de paternidad reclamada, disputada o indiscutible, además de exclusión de maternidad. Su utilidad es tal, que hace aproximádamente 3 años permitió en California confirmar la paternidad diferente en dos niños hermanos, nacidos de la misma madre y el mismo día, producidos por dos fecundaciones consecutivas de un negro y un blanco. Estudios antropológicos y estudios de secreciones corpóreas y manchas de sangre son de utilidad para distintos procesos judiciales. Su empleo en la filiación de inmigrantes ha sido de utilidad en Norteamérica para determinar la relación legal de los que solicitan la entrada al país, como lo sucedido con inmigrantes chinos.[8]

Grupos Sanguíneos

La sangre está compuesta por cuatro componentes: eritrocitos, leucocitos, plaquetas y plasma. Cada uno de ellos posee caracteres inmunológicos o fisicoquímicos característicos que vienen determinados por genes en forma específica que reciben el nombre de alotipo, fenotipo o simplemente tipos. En la Tabla I se enumeran los tipos conocidos y de utilidad en pruebas de filiación.

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TABLA I

Probabilidad de Exclusión - Inclusión

Sistema	Exclusión Simple	%	Exclusión Combinada	
1. ABO	20		20	
2. MNS	32		45.6	
3. Rh - Hr	29		61.4	
4. Kell	4		62.9	
5. Duffy	18.4		69.7	
6. Kidd	18.7		75.4	
7. Lutheran	3.6		76.3	
8. P	4		77.2	
9. X g^d	5		78.3	
10. Se	4	(I) =	79.2	
11. AcPl	25		25	
12. PGM 1	14.5		35.9	
13. ADA	5.8		39.6	
14. AK	3.3		41.6	
15. PGO	2.1		42.8	
16. GPT	18.6	(II) =	55.5	90.33%
17. GM	20		20	
18. Inv.	5.7		24.6	
19. Hp	18		38.1	
20. Gc	16		48	
21. C_3	13.8		55.2	
22. Ag X	14.3		61.6	
23. Tf	1	(III) =	62	96.3%
24. HLA	98.6	(IV) =	98.6	98.6%

Probabilidad Acumulativa:

1 + IV = 99;71% 1 + III = 99.23%
1 + II + III + IV = 99;9989 1 + II + III = 99;93%

Las plaquetas y la hemoglobina presentan también especificidad de grupo, sin embargo su empleo en casos de filiación, al presente, es escaso. No todos los antígenos conocidos se utilizan para las pruebas de paternidad, como se detalla en la Tabla II. Otros marcadores utilizados lo son enzimas eritrocitarias y proteínas séricas.

TABLA II

Componente Sanguineo	Sistemas		Especificidad	
	Conocido	Empleado	Conocido	Empleado
Antígenos Eritrocitarios	14	9	260+	24+
Enzimas Eritrocitarios	12	6	55	11
Proteínas Plasmáticas	13	7	90+	13
Antígenos Leucocitarios	3	1	24	21

Herencia de los Sistema de Grupos Sanguíneos

Los genes responsables de los grupos sanguíneos se heredan en pares siguiendo las Leyes de Herencia Mendeliana proveniendo uno de cada padre. Cuando ambos son idénticos hablamos de *homocigotos,* como AA, BB, Fy^a Fy^a, y de *heterocigotos* cuando ambos son diferentes: OA, AB, Kk, Fy^a, Fy_b.

La determinación de zigocidad puede ser demostrada en las células somáticas mediante distintas técnicas, como son: utilizando antisueros contra antígenos alélicos como por ejemplo anti-K, técnicas de titulación y conteo comparativo, por el número y localización de bandas electroforéticas y estudiando otros miembros de la familia. Las pruebas de filiación obligan al estudio de la madre, el niño, y el supuesto padre, o cuando menos el del niño y el padre cuando hay algún factor excluyente.

La detección de los grupos sanguíneos se realizan mediante técnicas simples aglutinación de sueros y células específicas que definen los antígenos de cada sujeto. La tabla III muestra los distintos componentes y datos básicos del sistema ABO. En el sistema Rh se incluyen las nomenclaturas de Wiener y Fisher (Tabla IV). La tabla V muestra las posibles combinaciones de Rh.

TABLA III

Combinaciones A B O

Grupos		
Padres	Posibles	Imposibles
O × O	O	A, B, AB
O × A	O,A	B, A B
A × A	O, A	B, A B
O × B	O, B	A, A B
B × B	O, B	A, A B
A × B	O, A, B, A B	NINGUNO
O × A B	A, B	O, A B
A × A B	A, B, A B	O
B × A B	A, B, A B	O
A B × A B	A, B, A B	O

Exclusiones

Hay tres formas de exclusión en casos de filiación en controversia: exclusión directa, indirecta y ligamientos de grupos sanguíneos.

La exclusión directa está basada en la presencia o ausencia de factores sanguíneos determinados por examen directo:

a. El niño presenta un factor sanguíneo que no está presente en uno o ambos padres.

Padre en cuestión	CW Negativo	*Exclusión*
Madre	CW Negativo	
Niño	CW Positivo	

El factor de Rh Cw no es observado en ninguno de los padres los cuales son Cw negativos. el niño es Cw positivo y es hijo obligado de la madre analizada, por lo que dicho

TABLA IV

Conversión Sistema Rh - Hr y D C E

Nomenclatura	
Wiener	Fisher-Race
FACTORES SANGUINEOS	
Rho	D
rh'	C
rh"	E
hr'	c
hr"	e
hr	f
TIPOS RH	
rh	cde
rh'	Cde
rh"	cdE
rhy	CdE
Rho	cDe
Rh 1	CDe
Rh 2	cDE
Rh 7	CDE

antígeno Cw positivo debe provenir de otro varón, excluyendo por tanto al objeto acusado.

b. El niño no presenta un factor que el padre en cuestión tiene que transmitirle por obligación:

Padre en cuestión	AB	*Exclusión*
Madre	O	
Niño	O	

El niño muestra ausencia de antígenos A o B y el padre en cuestión sólo podría transmitirle uno de los dos, excluyendo por tanto responsabilidad paternal en este caso.

La exclusión indirecta se basa en el estudio de genotipos homocigóticos:

a. El niño presenta un gen en forma homocigota que no se encuentra presente en ambos padres:

Padre en cuestión	kk	*Exclusión*
Madre	Kk	
Hijo	KK	

b. El niño no presenta un gen para el cual el supuesto padre es homocigoto:

Padre en cuestión	KK	*Exclusión*
Madre	kk	
Hijo	kk	

Una tercera forma de exclusión lo es por el ligamiento entre grupos sanguíneos. Algunos grupos sanguíneos están determinados por genes muy próximos entre sí, que se transmiten (segregan) casi siempre asociados. Estudiando otros niños de la misma pareja se puede determinar la segregación en el conjunto familiar en cuestión y determinar si un hijo en particular puede ser o no de la misma pareja. Usualmente este tipo de determinación no es frecuente en los casos de paternidad disputada, salvo en alegatos de paternidad para demandas de divorcio. Así observamos el siguiente ejemplo:

Padre		Madre	
MNSs		MSs	
MsNS		MS-MS	
Hijos			
#1	#2	#3	#4
MS-NS	MS-NS	Ms-Ms	Ms-Ns

En este conjunto familiar se observa que desde el punto de vista del padre, el antígeno M se transmite en los primeros tres hijos asociados a "s" y "N" asociados con "S". Por ello, el grupo MNSs del cuarto niño es tal que si el supuesto padre no es excluido, otro hombre tiene que ser el padre de los primeros tres hijos. El cuarto niño tiene Ms que proviene obviamente de la madre, por lo que debe haber recibido Ns del padre. El supuesto padre en este caso no podría proveer NS, por lo que se excluye su responsabilidad en este niño, justificando la demanda de divorcio.

Los antígenos eritrocitarios de los siguientes grupos y sistemas son los más utilizados en la determinación de filiación: ABO, Rh-Hr, MNSs, Kell, Lutheran, Kidd, P y Xg^a. No basta con saber si el individuo es Rh negativo o positivo, sino determinar los subgrupos del sistema Rh-Hr. El antígeno Xg^a tan sólo sirve para la exclusión de varones de la paternidad de hembras. Un hombre Xg (a+) no puede tener una hija Xg (a-), y un hombre Xg (a-) no puede engendrar una niña Xg (a+) si la madre es Xg (a-).[12]

TABLA V

Esquema de Posibles Combinaciones del Factor Rh

	cde	CDE	cDE	CdE	CDe	cdE	cDe	Cde
Cde	Cde/cde	Cde/CDE	Cde/cDE	Cde/CdE	Cde/CDe	Cde/cdE	Cde/cDe	Cde/Cde
cDe	cDe/cde	cDe/CDE	cDe/cDE	cDe/CdE	cDe/CDe	cDe/cdE	cDe/cDe	
cdE	cdE/cde	cdE/CDE	cdE/cDE	cdE/CdE	cdE/CDe	cdE/cdE		
CDe	CDe/cde	CDe/CDE	CDe/cDE	CDe/CdE	CDe/CDe			
CdE	CdE/cde	CdE/CDE	CdE/cDE	CdE/CdE				
cDE	cDE/cde	cDE/CDE	cDE/cDE					
CDE	CDE/cde	CDE/CDE						
cde	cde/cde							

Análisis de los resultados

La interpretación de los datos debe de ser correcta y tenerse en cuenta todos los factores de error para descartarlos.

1. *Calidad de los reactivos:* Debe asegurarse un control de calidad con técnicas adecuadas, controles adecuados, etc.
2. *Variaciones Fisológicas:* Tener en cuenta variaciones por edad, etc., al interpretar los resultados. Así por ejemplo, el antígeno A_1, puede no desarrollarse por completo hasta el año de edad; por ello, cuando esté envuelto el mismo en una filiación, se debe de esperar hasta que el niño cumpla dicha edad. Los antígenos "I" e "i" de Lewis no deben ser empleados para disputas de paternidad. Otros factores podrían ser antígenos adquiridos, enfermedades que modifiquen los antígenos, etc.
3. *Variaciones genéticas:* La presencia de mutaciones, sobre cruce ("crossing over") y anomalías cromosomicas podrían dar resultados no esperados. Sin embargo, estos son raros y hay formas de detectarlos en caso de que esten presentes.
4. *Problemas específicos de cada grupo:*

A- Sistema ABO

Fenotipo Bombay (Oh). Individuos homocigóticos para el gen h, por ejemplo hh no presentan el antígeno esperado A o B que puede ser observado en los descendientes que son heterocigotos Hh. Este tipo de grupo sanguíneo puede ser reconocido si el suero de los sujetos es analizado con células A, B y O. El fenotipo Bombay tiene anti-A, anti-B, y anti-H en su suero que reaccionará con células normales O.

Los resultados observados serían:

Células	Suero		Células		Reactivo
	Bombay	O Normal	Bombay	O Normal	
A	+++	+++	—	—	Anti-A
B	+++	+++	—	—	Anti-B
O	+++	—	—	—	Anti-AB
			—	+	Anti-H

2. Individuos con AB/O. Situación extremadamente rara donde A y B están en el mismo cromosoma.
3. Variantes débiles de A y B. Raro. Existen sujetos con antígenos débiles que sólo pueden ser detectados por la ausencia de una aglutinina esperada, utilizando anti-A, B(O), analizando secreciones o realizando estudios de absorción y elución.

B- Sistema Rh-Hr

La determinación de positividad o negatividad para el factor Rh (con antígeno anti-D) sólo permitirá la exclusión en el caso de un niño Rh+ de una pareja donde ambos progenitores sean Rh negativos, lo cual ocurre tan sólo en el 2% de los embarazos. Utilizando los antígenos anti-C, -D, -E, -c, -c, -e, -Cw y V, permite estudiar los subgrupos con una elevada probabilidad de exclusión.

1. Fenómeno de delección como -D-, Rh nulo, etc. deben de tomarse en cuenta cuando los resultados no son los esperados. Estudios cuantitativos permiten la aclaración al ser el antígeno D de mayor potencia que lo normal.
2. La disminución de antígenos puede dar falsos resultados cuando se emplean antisueros débiles; así por ejemplo; individuos Rn y (C) D (e) aparentan ser -D- pero la misma no se manifiesta.
3. Variaciones de antígenos que no reaccionan con sueros supuestamente específicos. Así observamos en Negros V (ce^a) o VS (e^a) positivos que darán resultados negativos o débiles con anti-hr" (e). Ellos deben ser analizados con técnicas más sensitivas de oficina. La exclusión de paternidad en el Negro basada en los variantes de los antígenos de Rh e y C debe evaluarse con cuidado.

C- Sistema MNss

1. Antígeno M^g - m Antígeno raro que puede ser identificado con anti-M^g; sin embargo, una persona M^gN aparentaría ser NN cuadno se utilice anti-M y N. Occure lo mismo con un individuo M^gM que aparentara ser MM.

Ejemplo del sistema MN cuando un padre M-negativo, N-positivo, y el niño es N-positivo:

	Anti-M	N	Mg	Fenotipo	Genotipo
Padre	0	+	+	N	M^gN
Madre	+	0	0	M	MM
Niño	+	0	+	M	M^gM

Una exclusión aparente basándose en el grupo MM se invalida si el niño y el padre son M^g positivos. Es un sistema raro (1 en 44.000). Este factor no excluiría la paternidad, sino más bien la incluiría. En todas las exclusiones por Mn la sangre debe de ser analizada para el factor M^g.

2. Antígeno M^k, similar al M^g pero no existe anti-M^k.
3. Antígeno Su. Un alelo de S o s, o un inhibidor que suprime S o s. Común en negros y responsable de la ausencia de S o s.

D- Fenotipos Menos - Menos

La mayor parte de los sujetos tienen por lo menos un antígeno de cada uno de los sistemas; sin embargo, se ha observado eritrocitos que carecen ambos antígenos del sistema Kell, Lutheran, Duffy, Kidd y del sistema S. Se les conoce como "fenotipos Menos-Menos". La ausencia de expresión del antígeno puede ser debida a supresión, delección, inversión o traslocación, o debido a un antígeno presente contra el cual no se conoce el anticuerpo. Ejemplos incluyen P, Lu (a-b-), Ko, Jk (a-b-), Fy (a-b-).

Este fenotipo ha de ser considerado en los casos de exclusión indirecta en que el niño debe de tener un factor que le debe transmitir su padre.

Enzimas Eritrocitarias en Pruebas de Filiación

Los hemolizados de hematíes contienen sistemas enzimáticos polimórficos que constituyen marcadores familiares específicos de gran utilidad para estudios poblacionales y de filiación. Los alelos de fosfatasa ácida, fosfoglucomotasa y transaminasa glutámicopirúvica son heredados en forma codominante. Los alelos de la glucosa —6 fosfatasa— dehidrogenasa son muy útiles al estudiar sujetos de ascendencia Mediterránea y Negra. Esta última enzima se hereda en forma ligada a X, por lo que su interpretación es válida tan solo en hembras.

A pesar de que las hemoglobinas no son enzimas, las mismas son proteínas polimorfas detectables en hemolizados eritrocitarios. La detección de ciertos tipos de hemoglobinas puede ser útil en casos de paternidad de ciertas razas, por ejemplo Negros (hemoglobina S) o cuando hay ciertas afecciones familiares con hemoglobinas anormales para casos de inclusión.

Proteínas Séricas

El polimorfismo de las proteínas séricas permite su empleo en la identificación de sujetos y pruebas de filiación. Existen múltiples proteínas séricas que podrían ser empleadas, pero en un número de ellas la variabilidad sólo se observa en algunos grupos étnicos donde se limita su uso (ej. - albúmina de México se observa en el 7.3% de los Indios Pima; albúmina de Noskapi en el 4% de los Ojibwas) para pruebas de filiación en la actualidad. Hay ocho variantes de albúmina, pero en los Caucásicos tiene poco interés ya que se presentan con una frecuencia de 1 en 10,000.

La determinación de céruloplasmina puede ser útil en Negros donde existe polimorfismo en un 4% de ellos. La transferrina puede ser de utilidad en ciertas poblaciones de indios americanos y negros.

Las dos proteínas más empleadas, debido a su distribución amplia, son la globulina Gc (componente grupo-específico) y la haptoglobina. El componente grupo-específico presenta tres fenotipos distintos (1-1, 2-1, 2-2). La frecuencia de los diferentes alelos varía entre las poblaciones Negra y la Caucásica.

Los factores GM son debidos a variaciones peptídeas de cadena pesada de la molécula IgG. Los factores Inv son debidos a diferencia en estructura de las cadenas livianas Kappa de las moléculas de inmunoglobulinas. Hay otros dos sistemas de la molécula Ig que han sido descritos: el marcador AM- que está ligado a el GM y el marcador isf que se hereda independientemente. Al presente se conocen más de 18 factores GM y S factor INV.[13] Los factores GM no se distribuyen al azar, sino que se presentan en combinaciones que varían con las razas. Estos complejos génicos se conocen como fenogrupos, alogrupos o haplotipos. La frecuencia de individuos INV positivos varía con las razas, estando presente en el 10-20% de Caucásicos, 50% de Negros y 60% de los Orientales.

Un factor importante a tener en cuenta en estas determinaciones de inmunoglobulinas es la edad del sujeto, ya que los niños menores de cuatro a seis meses tienen IgG predominantemente de la madre, por lo que el genotipo GM puede reflejarse por la presencia de IgG materna.

Antígenos de Histocompatibilidad (HLA)

Anticuerpos antileucocitarios fueron observados en 1955, siendo de tipo inmune. Al presente constituyen el grupo de más interés no solo desde el punto de vista de su capacidad de exlusión-inclusión en casos de filiación, sino también para la identificación de sujetos para transplantes compatibles de órganos. Al presente se pueden determinar más de 104 posibles haplotipos, con aproximádamente 8000 genotipos y 4000 fenotipos.[15-16] Se sabe que los genes que los determinan están localizados en el cromosoma 6 y que existe variabilidad entre razas en cuanto a los alelos más frecuentes. Existen varios métodos para su detección. La mayor parte emplean la aglutinación de leucocitos, citotoxicidad de leucocitos o fijación de complementos por plaquetas. Por ello se requieren muestras frescas con células blancas intactas (a excepción de la fijación de complemento plaquetaria) lo que limita su disponibilidad si el laboratorio que ha de procesar las muestras se encuentra a gran distancia. Se requieren antisueros específicos y al presente resulta una determinación cara y no realizada por los laboratorios de rutina. (Tabla VI). Su empleo permite la exclusión-inclusión con 98% de probabilidad, por lo que ha de convertirse en la prueba más útil de filiación. En nuestras manos ha permitido un grado de inclusión-exclusión de 99% de probabilidades con otras pruebas.

TABLA VI

Alelos de HL - A	
Primera Serie	Segunda Serie
HL- A 1	HL- A 5
HL- A 2	HL- A 7
HL- A 3	HL- A 8
HL- A 9	HL- A 12
W- 23	HL- A 13
W 24	W 5
HL 10	W 10
W 25	W 14
W 26	W 15
HL- A 11	W 16
W 19	W 17
W 29	W 18
W 30	W 21
W 31	W 22
W 32	W 27
W 28	

Determinación de Filiación

Utilizando los sistemas antes descritos se puede lograr excluir un sujeto acusado de un caso de paternidad, y si se obtienen datos de inclusión con una probabilidad mayor del 95% podemos asumir o incluir la paternidad, ya que esta cifra tiene amplia significación estadística. Este grado de certeza con frecuencia es difícil de obtener debido a la escasez de laboratorios que realicen todas las pruebas y al elevado costo de las mismas.

La seguridad de la paternidad nunca podrá ser afirmada

categóricamente. Sin embargo, si el niño y el padre en cuestión presentan uno o más marcadores en común, y la posibilidad de que esto ocurra es menos de uno en mil o uno en un millón con gran posibilidad el sujeto debe ser responsable. Al presente esta prueba es aceptada por múltiples cortes Europeas como definitivamente significativa.

La evidencia disponible que sugiere que el sujeto en cuestión es el padre real no es admitida al presente en nuestras cortes. Sin embargo, los datos estadísticos pueden mostrar su probabilidad de paternidad presentando datos que demuestren la rareza que no lo fuera, como se observa en el siguiente caso:

	A	B	C	D	E	c	e	M	N	S	s	Fy^a	Jk^a	Jk^b	Jp^a
Padre	0	+	0	+	+	+	+	+	+	+	+	+	+	+	+
Madre	0	0	0	0	0	+	+	+	0	0	+	0	+	+	0
Hijo	0	+	0	+	+	+	+	+	+	+	+	+	0	+	+

Con los grupos sanguíneos del niño y la madre solo 0.01% (1/10,000) hombres podrían ser compatibles con el padre de este niño. Este dato con el padre de este niño. Este dato constituye una fuerte evidencia de que el sujeto es el padre, aunque no lo pruebe con 100% de confiabilidad. Unido con otros datos puede permitir a la corte y al sujeto en sí asumir la paternidad.

Summary **Paternity testing has been under dispute for multiple years. Blood group detrminations has been of great help in identifying responsible subjects due to this specific genetic transmission.**

Advances in inmunohistochemical techniques has permitted the identification of multiple factors, of specific genetic transmission, that permits identification of subjects as well as compatibility of tissues.

With blood groups and HLA determinations inclusion-exclusion rates of paternity can be elicited with over 99% of probability. In this country jurisprudency has been established requiring blood group determinations in filiation cases.

A summary of the locally available techniques in our hands are included.

Por limitaciones de espacio se han excluido del artículo varios ejemplos de casos reales de determinación de paternidad en los que ha participado el autor. Los lectores interesados pueden solicitarlos a la dirección que aparece al calce en la primera página del manuscrito.

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NOTA DEL EDITOR: La madre, el niño, y el supuesto padre deben hacerse la prueba del antígeno leucocítico humano en casos de determinación de paternidad según dictaminó recientemente el Tribunal de Relaciones de Familia de la ciudad de Nueva York. El supuesto padre objetó la orden en base a la confiabilidad de la prueba, y que la misma violaba sus derechos de privacidad y de autoincriminarse.

El tribunal determinó que la prueba estaba incluida en la ley del Tribunal de Relaciones de Familia y que habría de respetar la decisión tomada por la Legislatura en relación con la confiabilidad científica de la misma. La prueba sanguínea no violaba el privilegio del padre de acogerse a la "Quinta Enmienda", ya que ésta aplica solo a casos criminales y no a casos de determinación de paternidad. Entendió el tribunal que el someterse a la prueba tampoco constituía una violación a su derecho de privacidad. El tribunal ordenó dividir en partes iguales los gastos de las pruebas.

Linda KL vs. Robert S., Tribunal de Relaciones de Familia, Nueva York, 22 de junio de 1981.
Citation vol 44(7)84, 1982.

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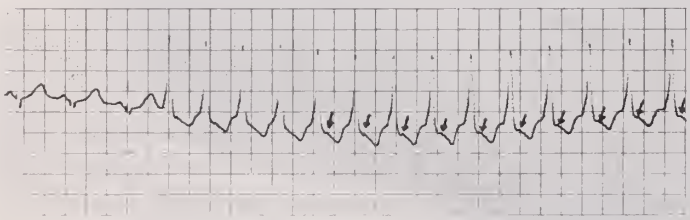
Sección de Auto Evaluación

ELECTROCARDIOGRAFIA PEDIATRICA

Rafael Villavicencio, MD

WPC es un niño de 2 años de edad referido para evaluación de un soplo cardíaco y ritmo irregular detectados por su Pediatra durante un examen físico de rutina. No había evidencia de infección reciente ni hallazgos en su historial médico pasado que sugiriesen fallo cardíaco.

Su crecimiento y desarrollo eran normales, y su tolerancia al ejercicio excelente. La radiografía de torax no demostraba cardiomegalia y los pulmones estaban libres de infiltrados. Durante un ECG de Holter de 24 horas se obtuvo el siguiente trazado.



El diagnóstico electrocardiográfico correcto es:

a) taquicardia sinusal
b) taquicardia supraventricular
c) sindrome de Wolff-Parkinson-White
d) taquicardia ventricular
e) fibrilación ventricular

Respuesta: d) Taquicardia Ventricular

Generalidades

La taquicardia ventricular (TV) se define como la presencia de tres o más extrasístoles ventriculares sucesivos. Estos suelen ser de comienzo súbito y terminación abrupta. Su frecuencia es variable, pero por lo general no es tan rápida como la taquicardia supraventricular (TSV) y puede ser crónica o en paroxismos.

En series recientes de TV en niños un 59% tenía un patrón de bloqueo completo de rama izquierda durante la taquicardia, 23% demostraban patrón de bloqueo de rama derecha, 12% tenían morfología indefinida y 12% presentaban patrón de bloqueo derecho e izquierdo.[1] En este último tipo de TV cambia gradualmente de bloqueo de rama derecha a bloqueo de rama izquierda (o viceversa) con complejos QRS casi normales durante la transición de un patrón a otro. A esta variante se le llama TV con "torsión de puntas" ("torsade de pointes") siendo esta morfología muy frecuente en intoxicación por quinidina y en pacientes con corazones sumamente afectados.

Criterios Diagnósticos

1) Intervalos R-R regulares
2) Frecuencia ventricular rápida (sobre 120/, min rara vez es mayor de 300/min)
3) Complejos QRS amplios y de morfología diferente a los QRS usuales.
4) Ondas P:
   a) pueden no estar visibles
   b) puede que su frecuencia sea menos que la del QRS y haya disociación atrio-ventricular. Esta disociación A-V está presente en la mayoría de los casos de TV en niños[2]
   c) pueden seguir a uno o todos los complejos QRS.
5) La observación previa de prematuros ventriculares en el trazado y de morfología similar a los complejos QRS de la taquicardia también suele considerarse de ayuda diagnóstica.

Mecanismo

Son los mismos que en la TSV:
1) por reentrada — los estudios electrofisiológicos invasivos en niños revelan que la mayoría de las TV son debido a una reentrada en el sistema de conducción ventricular[3]
2) por un automatismo anormal
3) provocadas por alguna disritmia

Salvo en una o dos excepciones la determinación del mecanismo específico de la TV no puede hacerse con un ECG de superficie. Para poder determinar con exactitud el mecanismo de la TV es necesario realizar estudios electrofisiológicos intracardíacos.

Análisis del Trazado

Los primeros tres latidos son de origen sinusal, a una frecuencia ventricular de 120/min., seguidos de TV a una frecuencia de 180/min. Pueden apreciarse los complejos QRS anchos (0.10 – 0.12 sec) y regulares. Desde el quinto

latido ventricular en adelante pueden identificarse ondas P (señaladas por las flechas)siguiendo los complejos QRS de una forma regular, manteniendo un intervalo P – P de 0.38 sec. Esta relación P-QRS indica disociación A-V.

Situaciones Clínicas

Las condiciones que más frecuentemente pueden ocasionar una **TV aguda** en niños con corazón normal son:

1) Procesos inflamatorios: miocarditis.
2) Agentes anestésicos: ciclopropano y flotano.
3) Factores mecánicos: cateteres y cables de marcapasos
4) Trastornos electrolíticos, hipoxia, e hipoglucemia
5) Medicamentos: digital, isoproterenol, quinidina, procainamida, fenotiazinas, y agentes simpatomiméticos.
6) Estimulantes como la cafeína, nicotina, y el alcohol.

En la mayoría de estos casos el pronóstico dependerá de la prontitud con que se pueda neutralizar el trastorno que precipitó la TV. En estas situaciones suelen convertir pronto y el pronóstico casi siempre es bueno, pero la posibilidad de que la TV se convierta en fibrilación ventricular (FV) debe tenerse siempre presente. En este último caso el pronóstico ya deja de ser bueno.

La TV crónica es rara en niños. En las series grandes 25% de ellas ocurrieron en niños con corazones normales, los cuales permanecieron asintomáticos casi en su totalidad[4] En los que desarrollan síncope éste puede ser por dis minución del débito debido a la frecuencia rápida o por conversión en FV. Esto es raro en niños con corazón normal, pues en ellos la TV con ritmo ventricular acelerados es muy bien tolerada.

Cuando la TV crónica aparece en niños con **corazones anormales** su pronóstico no es bueno y en ocasiones conduce a un desenlace fatal. Estas circunstancias ocurren más frecuentemente en niños con: miocardiopatías, síndrome de QT prolongado y en la tetralogía de Fallot post operada (2).

Evaluación de la Taquicardia Ventricular

A) Métodos no-invasivos

1) Historial — indagar sobre miocarditis en el pasado, descartar la presencia de algún factor causal (medicamentos, estimulantes, etc.)
2) Exámen físico — con un examen físico concienzudo puede detectarse la presencia de cardiopatías congénitas, adquiridas, o miocardiopatías que estuvieron desapercibidas.
3) El ecocardiograma y la radiografía de torax pueden revelar cardiomiopatías ocultas.
4) El ECG confirma la presencia de la disritmia, sus particularidades eléctricas y alteraciones asociadas como prolongación del intervalo QT, disociación A-V, etc.
5) El ECG ambulatorio continuo es mandatorio en un niño donde se quiere evaluar la magnitud de los extrasístoles ventriculares y descartar la posibilidad de una TV. Se debe tener en mente que la mayoría de las TV ocurren en niños asintomáticos con corazones normales.
6) Prueba de ejercicio — se recomienda en todo niño mayor de 4 años con extrasístoles ventriculares o cualquier otro tipo de disritmia ventricular. En niños con corazones normales la respuesta que característicamente se obtiene es que estos extrasístoles desaparecen durante el ejercicio para reaparecer en reposo en el periodo post ejercicio.

B) Métodos invasivos

Para confirmar el diagnóstico electrocardiográfico, evaluación del síncope, determinar las características de la taquicardia, su mecanismo, y recomendar el tratamiento óptimo de la TV, se llevan a cabo estos procedimientos. La técnica consiste de estimulación eléctrica programada del corazón y la provocación de múltiples extraestímulos ventriculares. Esto a su vez permite analizar la capacidad de los diferentes fármacos antiarrítmicos para prevenir la reaparición de TV.[5]

Tratamiento

A) Agudo

1) Corregir factores predisponentes (hipoxia, desbalance electrolítico, etc.)
2) Lidocaina 1mg/kg IV cada 5 min. por tres dosis. Puede seguirle un goteo endovenoso a base de 0.5 - 1.5 mg/kg/hr.
3) Atropina — si es TV con ritmo lento. La dosis recomendada es 0.01 mg/kg IV
4) Electroconversión sincronizada — comenzar a base de 0.5 a 1.5 Joules/kg e incrementar gradualmente hasta lograr la conversión.
5) Marcapasos de frecuencia programable principalmente en aquellas disritmias ventriculares hiperquinéticas refractarias.

B) Crónico

1) La presencia de extrasístoles uniformes (unifocales) y la TV en niños con corazón normal son en su mayoría disritmias de carácter benigno. Hasta hace poco se recomendaban diversos fármacos antiarrítmicos (propranolol; quinidina) en algunos casos pero su efectividad era mínima en estos niños. Actualmente en niños con TV crónica asintomáticos y con corazón normal solo se recomienda seguimiento médico de cerca sin utilizar medicamentos.[6]
2) En niños con corazones anormales y función miocárdica pobre, estas disritmias ventriculares son muy difíciles de tratar con éxito ya que la respuesta al medicamento dependerá del status hemodinámico cardíaco.

El medicamento de elección en pacientes con TV crónica y corazón anormal es la **fenitoína***. Se recomienda una dosis inicial de 4 mg/kg cada 6 horas por cuatro dosis. A esto le siguen 4 dosis de 2 mg/kg a intervalos de 6 horas tras lo cual se evalúa el ECG y se determina los niveles séricos del fármaco. Si hay una buena respuesta electrocardiográfica, con niveles séricos normales y sin que haya evidencia de hipotensión ni confusión mental entonces se ajusta la dosis de mantenimiento de fenitoína por vía oral. Usualmente se utiliza una dosis de mantenimiento de 2-4 mg/kg dos veces al día por vía oral.

Cabe aclarar que los pacientes con intervalo QT prolongdo y TV deben recibir propranolol. La quinidina está contraindicada (prolonga el intervalo QT) y el digoxin es usualmente infectivo en ellos.

* Dilantin.

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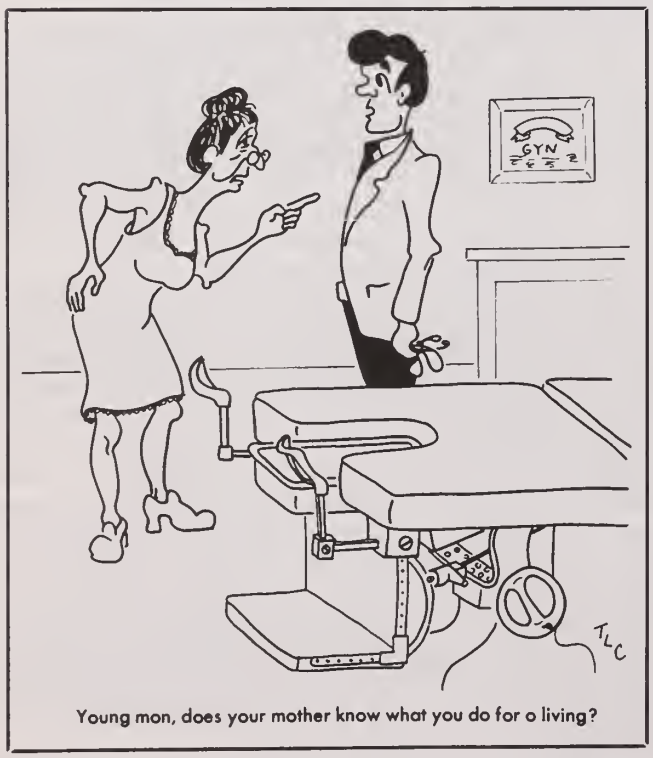

Young mon, does your mother know what you do for o living?

IMAGENES SONOGRAFICAS Y RADIOGRAFICAS

Manuel Pérez, MD

Clinical History

48 year old male admitted with three months history of decreased caliber of urine stream, and slight difficulty in voiding. Had a recent bout of hematuria, with suprapubic pain, and past history of renal lithiasis. Physical examination discloses an enlarged prostate.

Admission CBC, urinalysis, coagulation profile, serum electrolytes, BUN and uric acid were all normal. He had no hematuria on the admission urinalysis.

Figuere 1: Admission plain film of abdomen (KUB) shows several calcific densities overlying the medial aspect of the left iliac crest.

Radiology Department,
RAdiology Department,
Hospital Pavía, Santurce, Puerto Rico 00907

Figure 2: Bilateral retrograde pyelograms show a normal right sided collecting systems and ureter, with the right kidney in a normal position. The collecting systems on the left side are dilated and project over the iliac bone, with a short ureter and a malrotated kidney (facing anteriorly).

What is your diagnosis?

1. Left renal mass.
2. Ingested medication (opaque tablets).
3. Calcified mesenteric lymph nodes.
4. Nephrolithiasis in ectopic kidney.
5. Bilateral ureteral calculi.
6. Calcified myoma.

Diagnosis

Nephrolitiasis involving an ectopic (pelvic) left kidney.

Discussion

A pelvic (ectopic) kidney results from failure of renal ascent. At approximately the 14 and 30 mm stage of the

embryo, ascent of the kidney occurs. The kidney is formed by the union of uteric bud and the nephrogenic blastema caudally in the body. To attain the normal renal position in the adult, migration upwards outisde the pelvis must occur, as well as rotation. The renal pelvis, which originally lays in the ventral surface of the body (facing anteriorly), finally comes to face medially in the adult. At about the 25-30 mm stage in the embyro, the kidneys have reached their normal position on each side of the 2nd lumbar vertebra.

Non-visualization of a kidney in the usual flank position by excretory urography (IVP) demands close observation for a pelvic kidney because the calyces are frequently superimposed over the bony pelvis and difficult to detect. Clinically, an ectopic kidney may present as a pelvic mass. The differentation between a ptotic and an ectopic kidney is usually made by the short ureter in the ectopic kidney, as well as the degree of malrotation. Although clinically the diagnosis may be somewhat difficult, the ptotic kidney usually has a normal and high arterial supply.

Other anomalies of rotation include horseshoe kidney, where the lower poles are usually fused together; gross renal ectopia, in which the kidneys are fused and both kidneys lie on the same side.

To qualify as an ectopic kidney, the kidney must lie below the level of the 3rd lumbar vertebrae. There have been many pathologic conditions associated with ectopy. Hydronephrosis, stone, cyst, tuberculosis, and tumor have all been encountered in ectopic kidneys and may cause considerable confusion and difficuty in diagnosis. Other congenital malfromations of the genito-urinary tract have also been reported.

The diagnosis of an ectopic kidney may be done by intravenous urography, retrograde urography, ultrasonography and computerized tomography.

Suggested Reading

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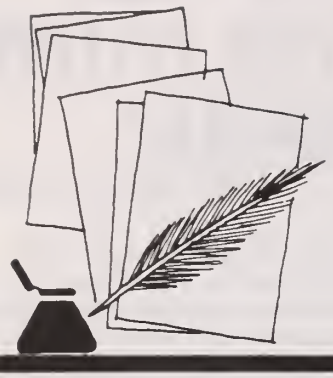

CARTAS AL EDITOR

El Ruego de un Anestesiólogo

Deseo solicitar de los internistas, de los médicos de familia y de los cirujanos, que comprendan la práctica de la anestesiología y cooperen con los anestesiólogos.

Muchos tienen en su mente una definición confusa de lo que es la anestesiología.

La anestesiología es el ejercicio de la medicina que se relaciona con los siguientes aspectos, pero no se circumscribe a éstos: (1) la utilización de los procedimientos necesarios para lograr que el paciente se torne insensible al dolor y a la tensión emocional mientras se le somete a una intervención quirúrgica, a un procedimiento obstétrico o a cierto tratamiento médico; (2) el sostenimiento de las funciones vitales mientras el paciente se encuentra sometido a las condiciones extremas producidas por las maniobras anestésicas, y quirúrgicas; (3) el tratamiento clínico del paciente sin conocimiento, sea cual sea la causa; (4) el manejo de los problemas relacionados con el alivio del dolor; (5) el manejo de los problemas relacionados con la resucitación cardíaca y respiratoria; (6) la aplicación de métodos específicos de terapia por inhalación; (7) el tratamiento clínico de diversos trastornos relacionados con los fluídos, electrolitos y metabolismo.

De los siete aspectos mencionados en la definición de la Junta Norteamericana Anestesiología (American Board of Anesthesiology), sólo dos se refieren estrictamente a actividades que se llevan a cabo en la sala de operaciones. Los anestesiólogos se han mantenido a la vanguardia en el campo del desarrollo y refinamiento de las técnicas de resucitación cardiopulmonar, de terapia respiratoria, de pulmonología aplicada y de cuidado médico de pacientes en estado crítico. Actuamos (o deberíamos actuar) como farmacólogos, fisiólogos e internistas de la sala de operaciones y de las secciones perioperatorias. Son anestesiólogos los directores de muchas de las más prestigiosas unidades de cuidado de pacientes en estado crítico. Somos, o deberíamos ser, expertos en el cuidado titulado de pacientes.

El temor de los internistas a perder el "control" de sus pacientes quizás sea la causa de que se dificulte el entendimiento entre aquellos y los anestesiólogos. En la lucha por establecer un mayor 'rapport', puede ser muy conveniente examinar algunos sucesos cuyo resultado podría ser el tratamiento inadecuado del paciente.

Un anestesiólogo puede planear un bloqueo subaracnoideo y, en la mañana de la intervención, descubrir que el internista o médico de familia ha administrado anticoagulantes al paciente. Excepto cuando se ha de administrar antibióticos, siempre se debe consultar al anestesiólogo antes de alterar en alguna forma sus instrucciones preanestéticas.

Sin consultar al anestesiólogo, el médico puede haber efectuado una digitalización acelerada de un paciente al que ya se le ha fijado la hora para anestesia e intervención. He tenido que posponer la anestesia de pacientes de avanzada edad intoxicados con digital mientras un internista les "preparaba" para la anestesia. ¿Cuánto más conveniente sería que el internista llamara al anestesiólogo y discutiera con él la necesidad de utilizar medicamentos para el sistema cardiovascular u otras drogas?

Se puede haber fijado la hora para la operación de un paciente que padezca de una severa enfermedad pulmonar crónica, sin la ventaja de que, antes de aplicar la anestesia, se haya consultado al anestesiólogo intensivista y sin que éste haya preparado al paciente. "Como resultado de la consulta previa, el paciente grave se beneficiará psicológica y fisiológicamente al percibir que un anestesiólogo experto y compasivo le ayudará a evitar todo contratiempo durante la operación".[1]

Es posible que un internista intente hasta prescribir el tipo de anestesia que se utilizará. Dripps y sus colegas[2] comentan brevemente este asunto: "Nos parece que el internista a quien se llama como consultor para evaluar la condición física de un paciente al que se ha de operar, lógicamente, no puede recomendar el tipo de anestesia o los agentes que se utilizarán". El bloqueo subaracnoideo puede ser el método anestético preferible para un paciente obeso e hipertenso que padece de una enfermedad pulmonar obstructiva crónica al cual se le practicará una ureterolitotomía baja, mientras que la anestesia general endotraqueal sería más conveniente para ese mismo paciente si se le fuera a practicar una colecistectomía. Un buen anestesiólogo se esfuerza por seleccionar el anestésico más conveniente para *este* paciente, que se someterá a *esta* operación, que practicará *este* cirujano, en *este* momento.

También se escucha el "insulto de los internistas", muy conocido por los anestesiólogos: "Induzca al paciente despacio, adminístrele gran cantidad de oxígeno y mantenga elevada la presión sanguínea. Debe utilizar el electrocardiógrafo durante la anestesia". En el mejor de los casos es inútil ofrecer este tipo de "consejo" a alguien que, por rutina, emplea drogas poderosas y potencialmente peligrosas, es experto en el uso de muchas clases de anestesia en pacientes

gravemente enfermos y vigila siempre las funciones vitales.

La anestesilogía del quirófano ha progresado mucho desde los días del "éter gota a gota". También hemos avanzado mucho más allá del argumento que aparentemente imaginan algunos de nuestros colegas: "la mitad de la jeringuilla grande, la jeringuilla pequeña completa y dos golpecitos hacia la derecha..."

Como poseedor de una vasta educación y experiencia en el campo de la medicina, puedo comprender la frustración que sufren algunos médicos al percatarse de que no pueden velar por su paciente ni en la sala de operaciones, ni en la sala de recuperación postanestética, ni, en algunos casos, en otras secciones de cuidado de pacientes en estado crítico. Hace doce años, cuando era un correcto médico residente, quedé asombrado al descubrir que un anestesiólogo decidiría si se podía internar a mi paciente en la unidad de cuidado intensivo. No obstante, los internistas y anestesiólogos tenemos que llegar a un acuerdo en lo relativo a nuestras respectivas responsabilidades para con los pacientes, tomando en consideración la pericia del anestesiólogo en materias como la resucitación, la adminsitración de fluidos, el equilibrio de ácidos y bases, las técnicas de observación continuada ("monitoreo"), el uso de medicamentos potentes, el cuidado respiratorio, el tratamiento médico de pacientes en estados crítico y diversas habilidades técnicas.

Los internistas tienen que percatarse de que los anestesiólogos son los expertos en anestesiología, para utilizar la redundancia. Deben proveer al anestesiólogo cualquier información que le pueda ser útil para el tratamiento del paciente durante el período perianestético. Es de escasa utilidad una afirmación como: "Se dictó la historia clínica y el examen físico; se da la autorización para la intervención." Si es útil preparar una "lista de problemas". Además, necesitamos saber cómo el paciente ha reaccionado a la tensión, si parece particularmente alérgico a algún medicamento, si ha tenido experiencias inusitadas relacioandas con la anestesia y las intervenciones quirúrgicas, cuáles son las razones para que haya utilizado medicamentos durante un período prolongado, etc. Si el paciente tiene problemas especiales, como una severa enfermedad pulmonar o un reciente infarto del miocardio, sería conveniente consultar con anticipación al anestesiólogo y que éste participara en el tratamiento preanestético del paciente. En muchas ocasiones, he podido mejorar la función pulmonar, por ejemplo, cuando se me ha solicitado que examine al paciente varios días antes de la fecha señalada para la intervención. Es insostenible que se pida a un anestesiólogo que asista a un paciente con feocromocitoma, sin que haya participado en su preparación preanestésica. También es inaceptable que se intente imponer el tipo o forma de anestesia que se utilizará. Por favor, recuerden la definición de anestesiología. Los anestesiólogos tienen mucho que ofrecer a vuestros pacientes y esperan que se logre una mayor armonía.

Dr. T. Cameron MacCaughelty
San Luis

1. *Vandam LD:* Anesthesiologists as clinicians. American Society of Anesthesiologistsa Rovenstine lecture, 1979, Anesthesiology 980; 53:40-48.
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Traducido de la sección *A Piece of My Mind*, JAMA, Dec. 11, 1981; Vol. 246. No. 23, por el Dr. Miguel Colón Morales, Director Depto. de Anestesiología y Terapia Respiratoria, Hospital del Maestro, Hato Rey, Puerto Rico.

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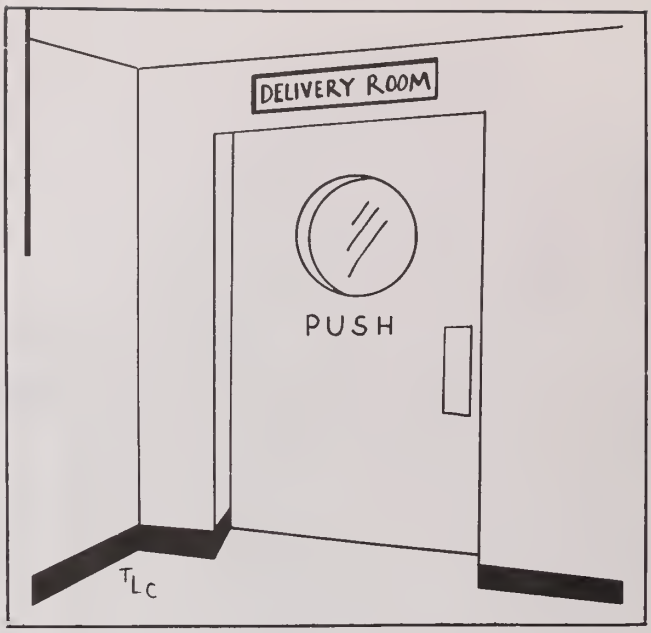

Resumenes de La Literatura Médica

EFICACIA Y SEGURIDAD DEL USO DEL AEROSOL DE ACETONIDA DE TRIAMCINOLONA EN EL ASMA BRONQUIAL CRONICA: Bernstein L., Chest 1982, 81. p.1.

El aerosol de acetonida de Triamicolona (TAA) y un aerosol placebo fueron comprobados en un estudio multicéntrico de 6 semanas de duración. El estudio incluyó 96 pacientes asmáticos que no recibían esteroides, los cuales fueron divididos y randomizados en dos grupos paralelos. Cada paciente se evaluó semanalmente con pruebas de función pulmonar (FEV, FVC, y FFF 22-25%). Al final de 4 semanas los pacientes tratados en TAA demostraron una mejoría significativa en comparación con los pacientes tratados con el aerosol de placebos los cuales su mejoría no fue significativa.

En los pacientes tratados con TAA la mejoría fue clasificada como excelente o buena en el 78% de los casos, mientras que ese grado de mejoría fue alcanzado solamente por el 24% de los pacientes tratados con placebo.

Luego de terminar las 4 semanas de tratamiento la mejoría observada en los pacientes tratados en TAA se redujo significativamente ($P < 001$). A ochenta y ocho pacientes se les continuó el tratamiento por un año durante el cual se registraron mejorías significativas en las pruebas de función pulmonar en los pacientes asmáticos evaluados cada dos meses. Los cambios en los niveles de cortisol plasmática no fueron significativos. Al final del estudio los investigadores hicieron una evaluación de la medicación de acuerdo a la respuesta de los pacientes. Las reacciones adversas fueron simples.

Ramón Figueroa-Lebrón, MD

INMEDIATE DETECTION OF EARLY HIGH RISK PATIENTS WITH ACUTE MYOCARDIAL INFARCTION USING TWO DIMENSIONAL EVALUATION OF LEFT VENTRICULAR REGIONAL LOW MOTION ABNORMALITIES: Howrowitz RS. Morganrouth J.; Am. Heart J. 103(5):814-822

In this study the authors evaluated 43 patients with an acute myocardial infarction that were studied with serial two dimensional echocardiography to define a high risk suspect for inhospital cardiovascular complications. This complications included pump failure, life threatening arrhythmias or death. A two dimensional echocardiography segments score was developed representing the extent of left ventricular regional wall motion abnormality which was correlated with peak total creatinine kinase release. Those patients that were studied that had a transmural myocardial infarction, had a segment score of 7.2, whereas those with a non-transmural myocardial infarction, had a segment score of 4.7. This difference was statistically. significant. Each total serum CK enzyme level level correlated statistically with segment score, but with a low correlation for coefficient. Forty percent of the 43 patients studied had an in-hospital complication and the segment score was 10 as compared to 4.6 in those patientes without a complication. A segment score greater than 8 was found in 11 of 13 patients who suffered a cardiac complications and in only 5 of the 30 patients without complications.

The patients' initial clinical classification was specific but very insensitive in predicting an early complicated course. In this study, the authors postulate that two-dimensional echorcardiography study of left ventricular regional wall motion can predict in the immediate post-acute myocardial infarction period the inhospital likehood of such patients developing a cardiovascular complication after the myocardial infarction.

COMMENTS: Although this study is interesting, it agrees with previous observations that the larger the involved area by the myocardial infarction, the greater the probability of subsequent complications.

Juan Aranda, MD

ELECTROPHYSIOLOGIC EFFECTS OF DISOPIRAMIDE PHOSPHATE IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME; Curr CR, Tristowski EN, Leith WM, Cook L, Gallaher J. Circulation; 1982. 65, (5):869-878.

Electrophysiologic studies were performed in 12 patients with the Wolff-Parkinson-White syndrome in order to evaluate the electrophysiologic effects of disopiramide phosphate. The sudies were performed during a control period and|after the intravenous administration of 0.05 mg per Kg of disopiramide over 40 minutes. This was followed by a continuous infusion of disopiramide 1 mg/Kg/hr. After the initial study, the patients were given the medications in doses ranging from 800-1200 mg/d for three days. After this period of time, the study was repeated. The study revealed that retrograde conduction through the accessory pathways was prolonged. However, although retrograde conduction through the accessory pathways was prolonged, disopiramide did not prevent the induction of supraventricular reentrant tachycardia. It was also found that disopiramide prolonged the shortest RR interval during atrial fibrillation. It was also

found that after oral disopiramide, the episodes of atrial fibrillation were shorter and self-terminating. No acute hemodynamic side-effects were observed in 5 patients developing gastrointestinal and anticholinergic side effects. Disopiramide appears to have beneficial electrophysiologic effects in patients with Wolf-Parkinson-White syndrome. Prolongation of refractoriness in the accessory pathways markedly slows the ventricular reponse during atrial fibillation and therefore prevents the development of life threatening arrhythmias.

Juan Aranda, MD

GALLBLADDER FUNCTION IN THE HUMAN FEMALE: EFFECT OF THE OVULATORY CYCLE, PREGNANCY, AND CONTRACEPTIVE STEROIDS: Everson GT, McKinley C, Lawson M, et al. Gastroenterology 1982; 82:711-9.

Las mujeres embarazadas o que usan píldoras anticonceptivas tienen un riesgo aumentado de desarrollar piedras de colesterol en la vesícula biliar. Los mecanismos de formación de piedras incluyen la secreción de bilis litogénica por el hígado y la formación de núcleos y de cristales de colesterol de esta bilis en la vesícula. Para la formación de piedras, entonces, es necesario retener bilis litogénica en la vesícula por algún tiempo. Los autores de este artículo midieron el volúmen de la vesícula biliar durante el día en mujeres saludables, mujeres embarazadas, y mujeres que habían usado píldoras anticonceptivas por un tiempo medio de tres años. Las medidas se hicieron con ultrasonografía. Se encontró que el volumen vesicular está aumentando durante todo el día en mujeres embarazadas y después de 12 horas de ayuno en mujeres en píldoras contraceptivas. El mayor volumen de la vesícula en estas mujeres representa retención de bilis y los autores postulan que esta retención puede contribuir al desarrollo de formación de piedras de colesterol.

Angel Olazabal, MD

EFFECT IF PSYLLIUM HYDROPHILIC MUCILLOID ON ORAL GLUCOSE TOLERANCE AND BREATH HYDROGEN IN POSTGASTRECTOMY PATIENTS: JD Welsh, CV Manion, WS Griffiths, and PC Bird Dig. Dis. Sci. 27:7-12, 1982.

La intolerancia en la prueba de absorción de glucosa fue común (75%) en 20 pacientes con historial previo de cirugía gástrica. La administración de psyllium junto con la comida disminuyó la hiperglucemica postprandial y disminuyó la hipoglucemia tardía. Estudios in vitro demonstraron que el material de psyllium retenía agua y glucosa. Los autores postulan que al dar psyllium con la dieta la absorción de carbohidratos es más lenta en el aparato digestivo aunque sigue siendo completa. Sugieren el uso de psyllium o sustancias con acción similar para tratar pacientes.

Angel Olazabal, MD

COARTACION AORTICA EN LA INFANCIA: Gutiérrez J., Gómez R., Cazzaniga M., et al. Rev. Esp. Cardiol. 1981; 34(6):515

La coartación aórtica en la infancia presenta controversia sobre el momento de la corrección quirúrgica. En el infante con insuficiencia cardíaca persistente la indicación para corrección es clara, no así la cirugía de otras anomalías asociadas.

Los autores analizan los resultados con las diferentes técnicas empleadas, la morbibilidad, y exponen sus criterios médico-quirúrgicos para esta malformación congénita.

Se consideraron 76 casos, lo que representa la experiencia de 2 años. La edad media era de 4.3 años de los cuales 56% eran menores de 6 meses.

De los 76 casos operados un 59% tenían coartación aislada y 41% presentaban otras anomalías como estenosis aórtica (15 casos) y comunicación interventricular (13 casos), otras fueron estenosis mitral, ostium primium con insuficiencia mitral, y transposición de las grandes arterias.

Las técnicas utilizadas fueron: anastomosis termino-terminal (12); aortoplastía con parche de "Gore-tex" (59); aortoplastía con colgajo de subclavia (4), y un caso con parche de Dacrón. No hay relación entre las técnicas usadas y la patología asociada o edad del paciente. La mortalidad global operatoria fue de 5.2% y la de coartación simple 2%.

Los autores recomiendan:

1. Un diagnóstico temprano y exacto de todas las lesiones con un estudio hemodinámico lo más completo posible.
2. Corrección precoz de la coartación sin límite de edad en los casos sintomáticos. Con las nuevas técnicas se reduce grandemente la posibilidad de recoartación. La cirugía temprana además evitará la aparición de hipertensión arterial y sus consecuencias.
3. Constricción quirúrgica de la arteria pulmonar ("banding") en los casos con comunicación interventricular (CIV) asociados.
4. Corrección en dos tiempos en los casos con estenosis aórtica asociada.

Insisten los autores que con el manejo médico-quirúrgico adecuado los resultados de la cirugía se pueden considerar excelentes. La mortalidad depende más de la malformación y situación clínica del enfermo que de su edad.

Rafael Villavicencio, MD

ENVENAMIENTO AGUDO POR THALLIUM: ESTUDIOS TOXICOLOGICOS Y MORFOLOGICOS DEL SISTEMA NERVIOSO: Davis L. E. Standefer, J. C., Kornfeld M., Abercrombie D.M., and Butler C. Ann Neurol 10:38-44, 1981.

El envenenamiento por Thallium es una forma rara pero significativa de neuropatía axonal aguda. Nueve días después de la ingestión de 5 a 10 gm. de nitrato de thallium, un hombre joven murió con neuropatías craneales y perifericas severas, anuria y fallo cardíaco. Exámenes ultraestructurales de los nervios hechos en los días 7 y 9 demostraron

degeneración axonal con pérdida de mielina secundaria. Los axones estaban hinchados y contenían mitocondrias y vacuolas distendidas. Los niveles de thallium en más de veinte órganos y fluídos corporales fluctuaron de menos de 1.0 a 178 microgramos/gm; concentraciones en veinte áreas del sistema nervioso fluctuaron de 29 a 140 microgramos/gm. Los niveles más altos en el cerebro se encontraron en la materia gris. En el tálamo, 87% del thallium estaba presente en la savia de la célula. Las concentraciones en los tejidos de thallium no eran paralelas a las reportadas para potasio, sugiriendo que la distribución de thallium en los humanos es diferente a la de potasio.

Manuel Naredo, MD

ESTUDIO ELECTRODIAGNOSTICO DEL SINDROME DEL TUNEL DEL CARPO DESPUES DE FACTURAS DE COLLES: Wainapel, S.F. Davis; L. Rogoff; J. B. Am J Phys Med 60:126-131, 1981.

Treinta y tres (33) pacientes con fracturas de Colles unilaterales fueron evaluadas por métodos clínicos y electrodiagnósticos para determinar la frecuencia concomitante de síndromes del túnel del carpo ipsilateral. En cuatro (4) pacientes (12.1%) se encontró que tenían el síndrome del túnel del carpo. La electrodiagnosis fue útil en confirmar y evaluar la severidad del envolvimiento del síndrome. La recuperación de la función de la mano no se vio afectada adversamente por la presencia del túnel del carpo. Debido a la incidencia significativa del síndrome del túnel del carpo en las fracturas de Colles, estos pacientes deben ser evaluados cuidadosamente ante la presencia de síntomas o signos que sugieran compresión del nervio mediano.

Manuel Naredo, M.D.

TRATAMIENTO DE MIELOMA MULTIPLE E INFECCION TEMPRANA: Perri et. al. Am. J. Med. 1981, 71:935.

El tratamiento de mieloma múltiple ha sido asociado con un aumento en la frecuencia de pulmonías penumocóccicas. Estudios recientes indican que también ocurre un aumento en la frecuencia de infecciones por organismos gram-negativos. Perri y colaboradores hicieron un estudio con 62 pacientes con mieloma múltiple que habían sido tratados con terapia inductiva con melphalan, predisona o BCNU, ciclofosfamida, y/o combinaciones de prednisona. Observaron 143 infecciones con una incidencia de 1.46 infecciones por paciente/año y 4.68 infecciones por paciente/año en los primeros dos meses de quimioterapia. Avanzado en el tratamiento, el riesgo de infección disminuyó a 1.04 infecciones por paciente/año e incluyó pacientes que se habían recuperado de infecciones iniciales,indicando que este sub-grupo no tenía mayor riesgo de recaída.

Las infecciones que ocurrieron temprano en el tratamiento con quimioterapia fueron causadas, en 15 casos por bacterias gram-positivas, y en 24 casos por bacterias gram-negativas; hubo infecciones mixtas en 2 casos. Al preparar cultivos, los organismos predominantes resultaron ser *Staphylococcus aureus, Streptococcus pneumoniae, Escherichia coli* y *Pseudomonas aeruginosa.* Predominaron las infecciones respiratorias (48%) y del tracto urinario (36%). Se encontraron hemocultivos positivos (blood isolates) en aproximadamente 25%. Hubo una tasa de mortalidad de un 17% en estas infecciones tempranas; hubo una tasa de mortalidad alta en pacientes con sepsis gram-negativa. La mortalidad se asoció también con niveles de creatinina de 2 mg/dl o más altos y con pacientes de 65 años o mayores.

COMENTARIOS: El mieloma múltiple se ha asociado con mal funcionamiento de anticuerpos que contribuye a infecciones tempranas con *S. pneumoniae.* La prednisona y los agentes citotóxicos suprimen los elementos de la médula ósea agravando así las anomalías inmunológicas y aumentando el riesgo de infección. Los primeros dos meses de terapia son críticos; esto es así debido a las dosis altas de quimioterapia y a que se utilizan otras modalidades terapéuticas en casos con complicaciones como hipercalcemia. Estamos de acuerdo con los autores en que los antibióticos profilácticos y la inmunoterapia en esta fase temprana de tratamiento para mieloma múltiple pueden ser útiles en la protección de los pacientes, pero, hasta el momento, no hay disponible un régimen definitivo o bien estudiado.

C. H. Ramírez-Ronda, M.D.

IMPORTANCIA CLINICA DE CAMPYLOBACTER JEJUNI: Blaser M. J., Reller, L. B.: N. Engl. J. Med. 1981, 305:1444.

Hasta hace poco, la mayoría de los casos de diarrea se consideraba eran causados por Salmonella, Shigella, *Escherichia coli,* cólera y/o amoeba. Mediante el uso de mejores técnicas de aislamiento se ha podido identificar a Rotavirus, Chlamydia. Yersinia y especie de Compylobacter como agentes etiológicos en casos de proctitis, colitis y diarrea. Actualmente la especie *C. jejuni* es reconocida como el patógeno principal de la enfermedad humana. Blaser y Reller hicieron una revisión de los hallazgos clínicos y de laboratorio de *Campylobacter enteritis.*

Las aves salvajes son los portadores principales de *C. jejuni,* pero también se han encontrado otros organismos que sirven de huéspedes a esta especie, tales como aves de crías a nivel comercial, cerdos, ganado, caballos y mascotas domésticos. La enfermedad se transmite por vía oro-fecal; por consumo de alimento y agua contaminada, y por contacto fecal directo del individuo afectado. La comida cocida, al igual que los alimentos y la leche pasteurizada no servirán de albergue a estos organismos.

C. jejuni tiene una distribución mundial, pero la incidencia mayor de este microorganismo ocurre en países sub-desarrollados. La mayoría de los casos ocurre en niños y en adultos jóvenes. *C. jejuni* es sensitiva a la barrera de ácido gástrico, y la ausencia de ácido hidroclórico puede predisponer a una infección. El organismo afecta el yeyuno, el íleo y el colon; produciendo reacciones sanguinolentas, edematosas y exudativas. En especímenes de biopsia rectal de algunos pacientes han aparecido patologías similares a las que se observan en la enfermedad de Crohn o en colitis ulcerativa.

Los síntomas son difíciles de diferenciar de los que se

observan en diarreas producidas por otros patógenos. La enfermedad puede ser severa y reincidente y puede ser bien similar a la colitis ulcerativa. La enfermedad comienza con fiebre persistente, seguida de dolor abdominal, náusea y diarrea con sangre. El dolor abdominal, en algunos casos, es tan severo que se asemeja a la apendicitis aguda, pero los signos peritonales son raros. la duración de la enfermedad se limita a una semana, pero en 20% de los casos el paciente sufre recaída o prolongación de la enfermedad. Se ha reportado megacolon tóxico, adenitis mesentérica y hemorragia en el área gastrointestinal baja, así como meningitis, convulsiones y artritis reactiva.

El dianóstico se hace observando la excreta en campo-oscuro (dark-field) o contraste de fase (phase-contrast). También es útil buscar leucocitos y eritrocitos en la excreta. El diagnóstico se confirma haciendo un cultivo de la excreta o haciendo cultivo de sangre utilizando un medio selectivo; este último método se utiliza con menos frecuencia.

La mayoría de los pacientes no requiere tratamiento, pero en casos de enfermedad prolongada o síntomas severos se requiere el uso de agentes antimicrobianos. Tratamiento con eritromicina (2 gramos por día dividida en 4 dosis, suministrada por vía oral) está indicado en la mayoría de los casos de enteritis. Otra alternativa conveniente sería doxicilina, mientras que gentamicina o cloramfenicol se han utilizado en el tratamiento de pacientes con enfermedades sistémicas y/o bacteremia.

C.H. Ramírez-Ronda, MD

"Just what exactly did you tell Mr. O'Toole about the hospital to get him to admit himself?"

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MSN MEDICAL SPECIALTIES NEWS

AMERICAN ACADEMY OF PEDIATRICS

WEIGHT LIFTING POSES DANGER TO TEENS

Teenagers could injure themselves through weight lifting, but weight training —a physical conditioning exercise— is reasonable safe for young adults, according to a new statement from the American Academy of Pediatrics (AAP).

The difference between these two methods of exercise is outlined in a statement written by the Academy's Committee on Sports Medicine.

In weight traininig, the athlete repetitively lifts weights which are lighter than his or her maximum capability. The exercise is an effective means of improving athletic performance in virtually all sports when done properly and, because it uses lighter weights, can be endorsed for teenagers, the Academy says.

In contrast, weight lifting is a competitive sport in which the athlete tries to lift the maximum weight of which he or she is capable and can only be done one time without an interval for rest.

Young people who lift weights "are extremely competitive and want to outdo their peers; therefore, they are prone to attempt lifts beyond their ability," says the Academy. Preadolescents should not participate in weight lifting, and teenagers who do so should be properly supervised.

The AAP points out that, according to the Consumer Product Safety Commission, 32,512 weight-lifting injuries required visits to hospital emergency rooms in 1979. Half of these injuries occurred to 10 to 19-year-olds, and the majority happened at home.

Injuries suffered by teenagers who lift weights include minor sprains and strains, fractures of longer bones, shoulder, low back and knee injuries, and "weight lifter's black-out", caused by a temporary decrease in blood reaching the brain.

A temporary but significant increase in blood pressure can also occur with weight training, making both activities dangerous to teenagers with poor cardiovascular systems or high blood pressure, the Academy says.

PEDIATRICIANS REAFFIRM NEED FOR PERTUSSIS VACCINE

The American Academy of Pediatrics reaffirmed its recommendation that young children should receive immunization against pertussis (whooping cough), and said that the risk of death and suffering caused by this highly infectious disease of infancy is far greater than the possible side effects of the vaccine.

The Academy was responding to an NBC-TV "Today" program which reported that dangerous reactions to pertussis immunizations are common. The Academy charged that the frequency and severity of side effects to the vaccine was disproportionately magnified in relation to the danger of this disease.

Said AAP President Glenn Austin. "The Today Show statement that 'serious reactions from the whooping cough vaccine are common... as low as one in 700 children' is untrue.

"In fact, the number of children innoculated with pertussis vaccine who have side effects such a high fever or convulsions is approximately 1 in 7,000. The number of cases of permanent brian damage is about 1 in 310,000 injections."

Dr. Austin said while it is true that side effects to children, including serious reactions, do occur in rare cases after innoculation, the use of pertussis vacine is responsible for the decline in the incidence of disease from 265,000 cases and 7,000 deaths per year forty years ago to 1,000-3,000 cases and 5-20 deaths per year now. He pointed to the dramatic rise in pertussis infections in England after 1974 when that country made adminsitration of the vaccine voluntary.

Dr. Austin also noted that in this country pertussis is still a killer, "and is itself a cause of brain damage and severe lung disease."

The Academy said that parents should be informed of the possible side effects of all vaccines and of the risk of the diseases by their physicians.

NATIONAL SOCIETY FOR MEDICAL RESEARCH

GAZELLES MAY HOLD CLUE TO POLYCYSTIC KIDNEY DISEASE

Until recently there were no known domestic or laboratory animals subject to polycystic kidney disease, which afflicts one of every 500 people in the United States. However, University of Florida researchers now have discovered that the disease does occur naturally among one group of animals, the South African Springbok gazelle.

A herd of 14 gazelles now is housed in Gainesville, where one of every four offspring dies from the disease. The researchers are looking for a marker to identify carriers of polycystic kidney disease among the gazelles and, possibly, among people. They also plant to investigate possible clues for prevention and treatment.

AMERICAN COLLEGE OF PHYSICIANS

ACP TAKES STEPS TO EDUCATE PHYSICIANS ABOUT NUCLEAR ACCIDENTS, WAR

A position paper on "The Medical Consequences of Radiation Accidents and Nuclear War" has been adopted by the American College of Physicians.

According to Dr. T. Frawley, President of the ACP, both the public and the medical profession need to know more

about the medical consequences of radiation accidents.

"The College, as an organization devoted to continuing medical education for physicians, accepts its share of the responsibility for promoting improved education about the medical consequences of radiation accidents," he said. "One Tuesday we will hold a special symposium on 'The Medical Consequences of Nuclear Accidents and Nuclear War.' We will provide physicians with materials from that program as an educational resource, the bibliography attached to our position paper also can serve as an excellent beginning point for physicians' self-education. Furthermore, we encourage individual physicians to tell the public about what happens to human bodies exposed to ionizing radiation."

Three important issues —treatment, education, and prevention— face physicians and the public with regard to radiation accidents and nuclear war, the ACP position says.

The ACP statement cites the problems faced by practicing physicians in the area around Harribsburg, PA, during the Three Mile Island incident as an example of the practicing physician's predicament in a radiation accident. Conflicting reports from industry and government made area residents distrust these two institutions. Fearful for their well being, persons turned to physicians for factual information and reassurance.

Practicing physicians, however, inundated with telephone calls from their patients requesting interpretation of the accident's significance in terms of their personal health —did not, however, have the immediate knowledge or expertise to give advice on the effects of ionizing radiation, the ACP position paper says.

The ACP maintains that medical education must be improved to increase and update the information physicians receive about the medical consequences of radiation accidents. It also urges that medical care professionals be trained to triage and treat blast, radiation, and burn injuries.

However, the College believes that there can be no adequate medical preparedness for the devastating medical consequences of nuclear war, Dr. Frawley said. "Prevention is the only reasonable medical response to the hazards posed by nuclear weapons," he declared.

Facts argue that medical disaster-planning for nuclear war —unlike that for radiation accidents— is futile, the ACP statement maintains.

This was proved, the ACP points out, by the situation after the nuclear blast suffered by Hiroshima in 1945. Sixty-five of the city's 150 physicians were killed outright, and most of the remainder were wounded. Of the 1,780 nurses, 1,654 were dead or too badly injured to work.

Whatever would be left of the American health care system after a similar blast would be assaulted by the need to provide short term teatment for untold numbers of fractures, organs ruptured from excess pressure, hemorrhage, and other trauma from flying glass and debris and long-term treatment for the injuries from radioactive fallout, the position paper says.

Most people exposed to radiation would die from central nervous system disorders, blood poisoning or from the effects of violent vomiting, diarrhea and hemorrhage, the ACP says. Those who survive would suffer extreme stress, trauma, fatigue, and burns. Over time, survivors would suffer an increased incidence of skin cancer, degenerative disease, accelerated aging, and problems of infertility, congenital malformations, still births, neonatal deaths, and genetic disase.

There is no possible adequate medical response to a situation where hundreds of thousands of people would be injured and ill, most hospitals destroyed, most medical personnel killed, and most medical suplies unavailable, the College says.

In closing, The American College of Physicians states its hope that public education of the medical consequences of nuclear war will raise the level of consciousness of the American people. The College also hopes that similar steps will be taken to elevate the awareness of the citizens of the Soviet Union and of all other nations bearing nuclear arms so that political leaders throughout the world will come to the bargaining table with identical mandates and incentives for success.

NONDRUG THERAPIES CAN BENEFIT ALL HYPERTENSIVES

All hypertensive patients, particularly those with mildly elevated blood pressure, should be placed on nondrug therapy, Norman Kaplan, MD, FACP, emphasized in a small-group educational session held during the American College of Physicians' (ACP) annual scientific meeting.

For patients with mild hypertension —defined as a diastolic pressure between 90 and 104 mm Hg —weight reduction and sodium restriction alone may control blood pressure so that drug therapy will be unnecessary or at least postponed, said Dr. Kaplan. For patients who do need medication to achieve adequate control, he said, addition of nondrug therapies to the regimen can potentiate the beneficial effects of drugs and ameliorate some of their negative effects.

Some patients may not be willing change their lifestyles to comply with a nondrug regimen, however, he observed. "Although they would rather be given medication and left with their bad habits," he said, "the prudent physician should present the best current evidence and encourage the patient to make changes that are feasible and potentially helpful."

Still, before any therapeutic approach is initiated in mild hypertension, the physician must first determine, through a series of multiple readings over time, that the patient actually does have hypertension, Dr. Kaplan said. Similarly repeated measurements also are necessary before the benefit of any type of therapy can be established, he cautioned.

A study conducted in Israel with moderately obese hypertensive patients provided good evidence that weight reduction can be accompanied by a significant fall in blood pressure, he said. The patients lost an average of 9.5 kg over four months and the average fall in blood prssure was about 30/20 mm Hg. This effect was independent of sodium restriction because urinary sodium content of those in the experimental group equaled that of patients in the control group, he noted.

In view of the frequent failure of dieters to maintain their loss, however, weight reduction alone is probably not sufficient for longterm blood pressure control in obese hypertensive patients, he pointed out.

Dr. Kaplan believes that excessive sodium intake is a likely cause of hypertension and that blood pressure can be significantly reduced by decreasing the usual daily intake of

150-200 mEq to 75-100 mEq.

This moderate level of sodium restriction is not hard to achieve if patients are instructed to eat more fresh and frozen foods and avoid canned and other processed foods that almost always have a high sodium content. Eating more fresh foods can also alleviate potassium loss in those who are on diuretic therapy.

Although there is no definitive evidence that regular isotonic or dynamic exercise helps reduce blood pressure, there is no reason to restrict these activities in patients with moderate hypertension, he said. Dr. Kaplan advocated advising patients to adopt a gradual approach to increasing levels of exertion and pointed out that some antihypertensive agents, such as beta blockers, may decrease a patient's exercise capacity.

Isometric or static exercise should be ruled out for hypertensive patients, according to Dr. Kaplan. Not only do they provide no lasting benefit, but the rise in pressure that accompanies isometric contractions could precipitate a vascular crisis, he warned.

Few of the various studies of behavioral relaxation techniques have shown a sustained effect on blood pressure reduction, but such therapies, along with daytime naps and adequate nightime sleep, could have some benefit for hypertensive patients.

Too much or too little alcohol may be harmful for the hypertensive patient, Dr. Kaplan said, citing the greater prevalence of hypertension in both teetotalers and in those whose alcohol intake averages more than 2 oz daily. Moderate intake of 1-2 oz per day, however, should probably be encouraged because it also has the side benefit of raising high density lipoprotein cholesterol, which has a cardioprotective effect, he said.

Dr. Kaplan advised physicians to turn to drug therapy in cases of uncomplicated hypertension only when diastolic remain at or above 100 mm HG after six months of nondrug therapy. If the diastolic pressure starts below 110 mm HG and decreases and stays below 100 mm HG, staying in good shape and restricting sodium may be all that's needed, he said.

Patients on nondrug regimens, however, need to be monitored just as closely as those on medication to make sure that the diastolic pressure does not rise above 110 mm Hg, at which point drug therapy is mandatory, he pointed out.

AMA NEWS

MDs REPORT ACTUAL PENICILLIN ALLERGIES RARE

Are you allergic to penicillin? Only about two percent of all patients are actually allergic to the drug, writes Irwin J. Polk, MD, MPH, in JAMA.

Penicillin allergy is frequently overreported by patients says Polk, a senior scientist in the AMA's Department of Drugs, replying to a physician's query about testing for penicillin allergy. It has been estimated that serious allergic reactions follow 10 to 40 of every 100,000 injections; only two of every 100,000 injections end fatally. Skin rashes and other reactions appearing in patients after administration of penicillin sometime occur in later stages of the viral infections for which the drug was prescribed, Polk explained in a separate interview.

In another response to the query, Richard D. DeSwarte, MD, states that currently available skin tests for penicillin allergy can detect sensitivity in some but not all potential reactors. New skin tests are being developed that will allow physicians to identify virtually all patients who are at risk of immediate allergic reaction to penicillin, adds DeSwarte, an allergist at the Rockford Clinic, Rockford, Ill.

STIMULANT MEDICATIONS MAY CAUSE TIC SYNDROME

Some children who take stimulant medications prescribed for hyperactivity are at risk for developing a severe tic disorder known as Gilles de la Tourette's syndrome, according to Thomas L. Rowe, MD, and colleagues from Yale University School of Medicine.

Tourette's syndrome is a neuropsychiatric disorder that appears in children from age 4 to 18 years. It is characterized by persistent motor tics (involuntary muscle twitches) and repeated vocal tics (involuntary sounds including grunting, barking, hissing, and shouting —often of repetitious sounds and obscenities).

As many as 500,000 children in the United States are taking stimulant medications for attention disorders. One in 1,500 —more than 300 children— may be particularly vulnerable to stimulant-induced Tourette's syndrome, either because of a genetic predisposition to the disorder or because their hyperactive behavior is actually an early symptom of Tourette's syndrome, says Rowe.

Treatment with stimulants can elicit tic symptoms in vulnerable children or worsen existing symptoms into a full-blown case of Tourette's syndrome, which may not be reversible even after the drug is discontinued, Rowe warns.

Rowe's group reports that 15 of 100 patients they evaluated for Tourette's syndrome developed the symptoms following use of stimulant medications (Dexedrine, Ritalin, or Cylert) originally prescribed for attention disorders. Discontinuing the stimulant medications and starting therapy with haloperidol (Haldol), a major tranquilizer, has decreased tic symptoms in some but not all of these patients.

The widespread use of stimulant medications may be increasing the incidence of Tourette's syndrome, Rowe speculates. Children with hyperactive or attention disorder symptoms need to be evaluated carefully for existing tics and Tourette's syndrome and for a family history of these conditions before a decision is made about beginning stimulant therapy, Rowe advises.

ELIMINATION OF MEASLES IN U.S. LIKELY BY OCTOBER 1982

A federal goal to eliminate measles in the United States by October 1982 is likely to be realized, according to a report from the Centers for Disease Control (CDC), Atlanta.

Citing CDC statistics, a group of investigators headed by Alan R. Hinman, MD, director of the Centers' immunization division, writes that the nation now is virtually free of measles. During the first 39 weeks of 1981, more than 90 percent of the nation's countries had no reported cases, and only 86 countries (2.7 percent) had reported measles more than twice during the years. A total of 2,668 cases was reported during the first 39 weeks of 1981, a 79 percent decrease from the incidence reported during the same period in 1980 and a 99.4 percent decrease compared to the same period in 1962, the year before maesles vaccine was licensed.

A nationwide childhood measles immunization program initiated in 1977 by the Department of Health, Education, and Welfare (now the Department of Health and Human Services) has made the most important contribution to the dramatic decline in measles, according to the CDC report.

Despite the extraordinary strides made in eliminating measles, the disease may be brought into the United State by people who have contracted measles in other countries and return home or visit while infected. CDC data from 1980 and 1981 indicate that these cases occur at the rate of about two per week. In recent months, United States citizens returning from abroad represent a high proportion of the imported cases.

Most imported cases of measles have not resulted in further outbreaks and appear not to threaten the elimination of measles in the United States. The fact that such cases do occur, however, indicates the need to maintain high immunization levels, continue surveillance and respond aggressively to reported cases, the CDC report warns. At present, in virtually every community in the United States, susceptible persons can receive measles vaccine free of charge at a local health department, the authors say. The vaccine also is available from private physicians.

"Achievement of the national target of measles elimination by October 1982 appears feasible", the CDC investigators conclude, "provided the current level of effort can be mantained."

ASPIRIN LINK TO REYE'S SYNDROME CREATING CONCERN, CONFUSION AMONG PARENTS

Recent articles reporting a link between aspirin use in children and Reye's syndrome have created problems for many parents who now wonder if they should continue to use aspirin to reduce children's fever.

Several weeks ago the Atlanta-based Centers for Disease Control (CDC) issued a warning that the use of salicylate-containing products (aspirin) to treat fevers in children with chicken pox or influenza shold be avoided if possible. The advisory was based on a statistical association between the administration of salicylates to chidren with either of these illnesses and subsequent occurrence of Reye's syndrome.

Reye's syndrome, named for Australian physican R.D.K. Reyes who first reported it in 1963, starts with a preliminary illness, usually a viral infection accompanied by fever, from which the child seems to recover. The child then relapses, and the syndrome itself is marked by vomiting, confusion and delirium, sometimes progressing to coma. Reye's syndrome can be fatal. According to the JAMA report, "the incidence of Reye's syndrome is not known, but probably ranges from less than one case per 100,000 children under the age of 18 years in a mild influenza B season to as much as two or three cases per 100,000 children in years of high influenza B activity... During the last ten years, the number of reported deaths from Reye's syndrome in the United States has ranged from about 60 to as high as 160 per year."

The CDC report said that, while studies indicate aspirin may be a factor in the development of Reye's syndrome, there is no proof that it actually causes the disorder.

The basis for the CDC advisory was a report from a panel of outside consultants asked by the CDC to review all studies linking aspirin and Reye's syndrome, including a recent one conducted by the Michigan Department of Public Health under epidemiologist Ronald Waldman, MD. The CDC's message, according to E. Russell Alexander, MD, chairman of the panel and an expert on pediatric infectious diseases at the University of Arizona in Tucson, is that "we're recommending caution in administering aspirin in a time and place where influenza and chicken pox are around."

Diane Rowley, MD, of the CDC staff, who worked with the panel in drafting the final statement, agrees that the warning should be considered in the context of the known strong association between Reye's and both chicken pox influenza.

"You have to consider in the early stages of a child's febrile illness (one associated with fever) whether it has been exposed to either disease and what is prevalent in your community," she told JAMA Medical News.

The CDC advisory has stirred up considerable confusion among both parents and physicians. Rowley reports receiving many calls from parents wanting to know what to use instead of aspirin. She says she tells them that "they may want to contact their child's physician before choosing to treat a fever," adding that, "in many children, a fever of 101 or 102 degrees may not be cause for alarm."

A husband and wife research team studying Reye's syndrome at the State University of New York at Stony Brook, Jacqueline Partin, MS, and John Partin, MD, Chairman of the Department of Pediatrics, recommend against using fever-reducing medication such as aspirin unless the temperature becomes very high. The degree of fever seen in chicken pox and influenza is not in itself dangerous and usually can be alleviated by cool sponging, Ms. Partin notes.

Aspirin's chief alternative is a cetaminophen. However, the CDC panel consultants did not recommend this agent because, "We didn't have the information about its risks and benefits," says Alexander. "We did suggest to the CDC that another group should look at that question."

COLERA ON THE TEXAS GULF COAST

Cholera, a disease marked by severe gastrointestinal symptoms, has made a reappearance in the low-lying coastal areas near the Gulf of Mexico, raising concern that the causative bacteria may be endemic to this region of the country.

Sporadic cases of cholera previously have been reported in Texas and Louisiana since 1973, after a sixty-year hiatus, according to an account of two recent cases in the March 19 issue JAMA.

A team of investigators, headed by Michael T. Kelly, MD, of the University of Texas Medical Branch at Galveston, found that water and mud samples taken from the vicinity where the two recently infected patients lived in Texas contained the offending organisms.

Even though both patients had been exposed to the water, the authors could not say with absolute certainty that this was the source of the patients' infection.

Most of the other recent cases of cholera in the United States have been associated with the consumption of raw oysters and inadequately cooked crabs, presumably taken from water supplies contaminated by sewage.

The JAMA authors' findings support the suggestion that the bacteria responsible for cholera may be capable of existing and multiplying in the Gulf Coast environment in a free-living form. If so, this means that cholera can be contracted directly from water sources in certain Texas coastal regions and not only from eating food contaminated with the responsible organism.

MARATHON RUNNING ALTERS FAT LEVELS IN THE BLOOD

Sustained exercise, such as marathon running, increases the body's level of high-density lipoprotein (HDL) and, therefore, may decrease the risk of heart disease, according to a study in the March 26 issue of JAMA.

A team of researchers led by Rudolph Dresendorfer, Ph.D., at the Human Performance Laboratory, University of California, Davis, found significantly increased HDL levels in 12 men participating in the 20-day, 312-mile Great Hawaiian Footrace. A high level of HDL has been linked to a lower cardiovascular mortality rate in studies at least since 1975.

The twelve runners, aged 23 to 60 years, ran an average of 17.3 miles per day for ten days, rested 70 hours, and then ran for eight more days. Blood samples taken throughout the 20-day period showed a significant increase in HDL levels on active running days and a decrease during the rest period.

The study shows that athletes who run long distances regularly can expect to enjoy similar beneficial results.

USE PROPRANOLOL FOR AT LEAST THREE YEARS AFTER HEART ATTACK, NIH REPORT RECOMMENDS

National Institutes of Health researchers are recommending that propranolol hydrochloride (Inderal), found last year to reduce deaths after heart attack by 26 percent, be prescribed for at least three years to patients who have survived a heart attack and can tolerate the drug.

The National Heart, Lung, and Blood Institute sponsored Beta-Blocker Heart Attack Trial (BHAT), conducted at more than 100 medical centers and hospitals from June 1978 to October 1981, was discontinued nine months ahead of schedule because results revealing the benefits of the drug were considered unequivocal. Mortality statistics from the final BHAT report and the investigators' recommendation appear in the March 16 issue of **JAMA**.

Propranolol hydrochloride is one of a class of drugs known as beta blockers that prevent certain nerve impulses from stimulating the heart, arteries, and lungs. As a result, the drug tends to reduce the heart rate and the force of heart muscle contraction, thereby decreasing the heart's work load and need for oxygen and reducing blood pressure. Because of these actions, propranool hydrochloride has been found effective in certain patients in treating hypertensoin and in reducing the frequency and intensity of chest pains from angina pectoris. Side effects can include bronchial spasm and reduced blood circulation in the extremities.

During the study period, 3,837 men and women, aged 30 to 69 years, who were hospitalized with a heart attack were randomly divided into two groups; one began receiving propranolol hydrochloride and the other a placebo. To prevent bias in the results, neither the physicians nor the patients knew which group received the active drug. The patients were monitored after discharge at regular intevals.

No serious side effects were associated with either propranolol hydrochloride or the placebo, although there were slightly more complaints of low blood pressure, gastrointestinal problems, tiredness, respiratory distress, and cold hands and feet among patients taking the drug. Rapid heart beat was more common among those taking the placebo.

After an average 25-month follow-up period, total mortality was 7.2 percent (138 patients) in the group receiving propranolol and 9.8 percent (188 patients) in the group receiving the placebo, an overall reduction in mortality of 26 percent for the group receiving the beta-blocker. "Regardless of whether the patients had had more than one MI [myocardial infarction, or heart attack], a single MI with complications..., or a single uncomplicated MI, propranolol was found to be efficacious," the report states. The beneficial effect of the drug seems more pronounced in the first 12 to 18 months following the heart attack, although the effect lasted throughout the time patients were followed, an average of 25 months and a maximum of 39 months.

Based on the BHAT results and findings of previously reported studies, the BHAT investigators recommend the use of propranolol for at least three years in patients who have had a recent heart attack and who do not have any other medical conditions that would exclude use of the drug.

"It is certainly comforting to know that beta-blockade will not only... improve angina pectoris, slow the heart rate, and lower the blood pressure, but will also prolong life in this group of patients," comments cardiologist, Richard J. Jones, MD, Director of the AMA's Division of Scientific Policy. "The finding will make it all the more desirable to develop more highly selective beta blockers that might be even more effective while causing fewer side effects," Jones says.

POTENTIAL DANGER FROM HUMAN BITE WOUNDS

Most human bite wounds are superficial and require no immediate measures except cleaning. However, the March 26 issue of **JAMA** contains a warning that such bites should be inspected daily for two or three days because of potentially serious consequences if infections should occur.

Infections from human bites are most frequently caused by *Streptococcus* and *Staphylococcus* organisms. Infected bite wounds may require antibiotics, treatment with antitetanus medications, or even surgery to ensure drainage if bite are deep, according to James W. Mosley, MD, of the University of Southern California School of Medicine, Los Angeles, replying to another physician's query regarding management of bite would in institutions for the mentally retarded.

Exposure to hepatitis B virus is a potential hazard of any human bite, but the risk is higher in facilities for the mentally retarded, Mosley notes. The hepatitis B carrier rate among persons with Down's syndrome may exceed 10% to 20%. When use of the new hepatitis B vaccine becomes routine, infections from the virus will be greatly reduced because the vaccine will confer lasting immunity.

"How many others feel that Bruce is undermining the therapy group by coming to the sessions dressed as a water buffalo?"

WORLD MEDICAL ASSOCIATION TO CONDUCT INTERNATIONAL CONTINUING MEDICAL EDUCATION (CME) MEETING

An international assemblage of physicians and medical educators is expected for the World Medical Association (WMA) Continuing Medical Education Meeting in Honolulu, Hawaii.

The WMA Meeting, to be held in conjunction with the 126th annual scientific meeting of the Hawaii Medical Association (HMA), will privide up-to-date continuing medical education on current topics of interest to physicians.

Among the topics to be discussed are "Evaluation of Methods of Continuing Medical Education", "Leprosy", "Current Advances in Pharmacotherapeutics", "Current Technologic Advances", "Health Care Manpower", and "Current Advances in the Disorders of the Central Nervous System".

The program offers a total of 19 hours of Category 1 Continuing Medical Education Credits.

A special feature will be the presentation of Live Clinics at various hospitals, and the use of Video Clinics, which are videocassette programs for continuing medical education, produced by the American Medical Association. The WMA registration fee is $50.

All physicians, medical educators and other interested health care personnel are encouraged to attend. For additional registration or program information, please contact the World medical Association, North American Region, 536 N. State Street, Chicago, IL 60610, or call Ms. Eva Stone, (312) 751-6230.

THE SECOND ANNUAL INTERNATIONAL SYSMPOSIM ON THE CLINICAL APPLICATIONS OF CARDIOPULMONARY IMAGING

Wednesday, September 29-
Saturday, October 2, 1982

Hyatt Lake Tahoe
Lake Tahoe, Nevada

Directors: Nicholas J. Fortuin, MD, Associate Professor of Medicine, Johns Hopkins University School of Medicine, and Director, Cardiac Graphics Laboratory, Johns Hopkins Hospital, Baltimore, Maryland

Frederick P. Stitik, MD, Professor of Radiology, Eastern Virginia Medical School, Norfolk, Virginia; Clinical Associate Professor of Radiology, Johns Hopkins University School of Medicine; and Chairman, Department of Radiology, DePaul Hospital, Norfolk, Virginia

This four-day cardiopulmonary course is designed for radiologists, cardiologists, pulmonary physicians, general internists, cardiothoracic surgeons, and other practitioners who desire a comprehensive "patient-oriented" learning experience in the newest cardiopulmonary imaging techniques.

The course will update and refine assessments of the different imaging techniques and their application to diagnosis and management of patients with cardiopulmonary diseases. Plain film techniques, echocardiography, radionuclide scanning, computed tomography, digital imaging, conventional arteriography, nuclear magnetic resonance, and interventional techniques will all undergo a detailed "when, where, why" scrutiny. A lecture/workshop/case-discussion format will be used to intensify the instruction on each modality in the imaging array. Manufacturer's exhibits of latest equipment will augment the formal instruction. Afternoons will be kept free for enjoyment of Lake Tahoe.

The course will have an outstanding faculty whose members have been chosen for their teaching ability as well as for their expertise in their assigned areas of instruction. Included will be Drs. Richard L. Popp, Eric Milne, Mark Wholey, Rogelio Moncada, Charles Higgins, Kenneth McKusick, William Roberts, and the course co-directors, Drs. Fortuin and Stitik.

For Further Information:

Contact Educational Resources Associates, Inc., P.O. Box 369, Brookline, Massachusetts (USA) 02146. Tel: (617) 738-8859 or 8861.

Accreditation:

AMA Category I: 24 hours

Tuition:

$375. Will include syllabus, cocktail party, and refreshments.

ANNUAL CONFERENCE OF AMERICAN MEDICAL WRITERS ASSOCIATION SCHEDULED FOR OCTOBER

New applications for word processors and the use of teleconferencing are two of the many topics slated for the 42nd Annual Conference of the American Medical Writers Association (AMWA) in Los Angeles, October 26-30, 1982.

Norman Cousins, noted author, editor and teacher, will speak at the Distinguished Guest Lecturer Luncheon on Wednesday, October 27; Melvin Figley, MD, editor of the *American Journal of Roentgenology* will talk about opportunities for journals and other print media; Barnett Addis, Phd, of the Neuropsychiatric Institute at UCLA, is a film producer and director who will speak on the continuing role of film and television. James Breeling, executive director of the American Dietetic Association, will describe his

organization's use of teleconferencing. The keynote address will be given by Phil Manning, MD, associate dean of continuing education at the University of Southern California.

Sixty workshops in writing, editing, design and audiovisual production —geared to basic, intermediate and advanced levels of skill— will be held at the conference. The courses at each AMWA conference are divided into fields of employment interest —public relations, freelance, editorial, audiovisual and pharmaceutical— with special meetings geared to those already employed in the various fields or interested in learning more about the subjects.

On Friday, October 29, the most advanced word processing equipment will be on display and writers will have a change to learn about how this technology can revolutionize everyday work.

A post-conference session "Diet Writing: The Trick and the Treat" will be given by R. Philip Smith and AMWA President, Theodore Berland on Sunday, October 31.

Registration fee for the conference is $50, or $25 for one day. Separate fees are charged for workshops.

The Department of Radiology
THE CHILDREN'S HOSPITAL MEDICAL CENTER
Harvard Medical School

Announces
The Annual Course in PEDIATRIC RADIOLOGY
November 1-3, 1982
Hyatt Regency Hotel, Cambridge, Massachusetts

Program Chairman: Dr. John A. Kirkpatrick, Jr.
Program Director: Dr. William J.H. Caldicott

This three-day coure will review the diagnostic and therapeutic imaging techniques employed in pediatric radiology, with emphasis on the application of these techniques to diagnostic problems in children. Designed to benefit a broad spectrum of physicians —general and diagnostic radiologists, skeletal radiologists, and other practitioners interested in pediatric radiology— the coverage will include roentgenography, radiologic special procedures, nuclear medicine, ultrasonography, and computed tomography. A varied teaching format will be used, to consist of lectures, workshops, discussion periods, and cases-of-the-day presentations. Daily luncheon arrangements, with faculty members and registrants seated together, will extend the opportunities for informal interchange.

Social events will include a cocktail reception and optional day tours and evening entertainments.

Faculty:

Drs. William J. H. Caldicott, Kenneth E. Fellows, Harvey V. Fineberg, N. Thorne Griscom, G.B. Clifton Harris, John A. Kirkpatrick, Jr., Robert L. Lebowitz, E.B.D. Neuhauser, Roy D. Strand, Rita L. Steele, Salvador Treves, Robert H. Wilkinson, and Roberta G. Williams.

Accreditation:

AMA Category 1: 22 hours

Tuition:

$3.65. Will include course syllabus, cocktail reception, lunches, continental breakfasts, and refreshments

For Further Information:

Contact Educational Resources Associates, Inc., P.O. Box 369, Brookline, MA (USA) 02146. Tel: (617) 738-8859

22nd ANNUAL POSTGRADUATE SEMINAR - "GLIMPSES FORWARD" - CLINICAL APPLICATIONS OF NEW DIAGNOSTIC IMAGING AND INTERVENTIONAL TECHNIQUES

November 11, 12, and 13, 1982

Held at Mount Sinai Medical Center of Greater Miami. Program Director: Manuel Viamonte, Jr., M.D. Physicians Fee: $150. - Residents and Fellows: $75. - Approved for Category I AMA - 16 credit hours.

For further information, please contact:

CME Coordinator, Department of Continuing Medical Education, 4300 Alton Road, Miami Beach, Florida 33140 - Telephone (305) 674-2311.

ASOCIACION LATINOAMERICANA DE DIABETES
V CONGRESO LATINOAMERICANO DE DIABETES

4 a 8 Abril de 1983, Santiago, Chile

Secretaría General, Chacabuco 419, 2do. Piso, Santiago, Chile

La Asociación Latinoamericana de Diabetes eligió a la ciudad de Santiago de Chile como sede del V Congreso Latinoamericano de Diabetes, evento a desarrollarse entre el 4 y 8 de Abril de 1983.

El Comité Directivo del Congreso al tomar esta responsabilidad, se fijó como objetivo organizar un torneo que logre no sólo excelencia científica, sino que sea motivo de unión y amistad entre todos los profesionales médicos y de colaboración médica que trabajan en Latinoamérica en el campo de la diabetes.

Con este doble espíritu invitan a concurrir a la cita de Santiago de Chile, a fin de alcanzar el éxito que la diabetología latinoamericana se merece. El brillo del V Congreso Latinoamericano no dependerá de este Comité Directivo, que es sólo un intermediario, sino del apoyo generoso que Uds. le brinden con su asistencia.

AMERICAN ACADEMY OF DERMATOLOGY

X PEDIATRIC DERMATOLOGY SEMINAR

The 10th Pediatric Dermatology Seminar will convene at the new Carillon Beach Hotel, Miami Beach, Florida, February 24-27, 1983. Guest Speakers will include: Yehudi Felman, Arthur Norins, Heinz Eichenwald, Arthur Rhodes, Guinter Kahn, Mark Dahl, Lawrence Schachner, etc. The seminar fee is $240.

A seventeen day post-seminar tour to China will visit Kweilin, Hangchow, Peking, Wuxi, Shangai, Suzhou, and Hong Kong. (All inclusive costs, $2395) CME credit is given.

For information contact: Guinter Kahn, M.D., 16800 N.W. 2 Ave. No. 401, Miami, Florida, 33168.

ROBERTO CLEMENTE:
Bronze Statue to be Erected in United States

A 9-foot heroic-size bronze sculpture of **Roberto Clemente** will be erected at Pittsburgh, PA's Three Rivers Stadium to honor the former Pirate player and humanitarian. A Limited Edition of 200 bronze replicas of the sculpture will be sold to raise the funds necessary to cast the larger bronze statue. The proceeds from the sale of the 12 1/2-inch high bronze sculpture will be used to cast the larger one instead of using public funds or government subsidies.

The bronze sculpture, by Malcolm Alexander, of Santa Barbara, Calif., has done many sports figures in bronze including Joe DiMaggio, Bob Lilly, George Blanda, Pancho Segura.

Each Clemente bronze will be cast in the Lost Wax Process so no two casts can be exact duplicates; each will be a true original. After the 200 have been sold, the molds will be destroyed so no others can be cast. Attesting to its status as an original Limited Edition bronze, a certificate of authenticity will be issued for the protection of the purchaser. In this way, the purchaser is assured of the rarity and monetary value of the bronze.

Edition Number 1/200 was given to Mrs. Vera Clemente, Roberto's Widow, and is now in the Roberto Clemente Museum in Sports City, San Juan. Edition Numbers 2/200, 3/200 and 4/200 will be presented to the Clemente sons at the stadium dedications.

A sales prospectus and information about the numbers that are left in the Limited Edition can be secured from the project coordinator, Kate Goodrow, in Pittsburgh, PA. Write to 9420 David Drive, Pittsburgh, PA 15237 or call (412) 367-4821. The price for the bronze sculpture is $1,655 each; interest-free payment plans are available, too.

CARDIO 82
Asociación Puertorriqueña del Corazón

SESION CIENTIFICA
5 y 6 de septiembre de 1982, Dorado Beach Hotel

La Asociación Puertorriqueña del Corazón tiene el placer de anunciar su próxima actividad científica anual - CARDIO-82 - con la participación de distinguidos cardiólogos visitantes en colaboración con cardiólogos locales. Esta actividad, co-auspiciada por la División de Educación Médica Continuada de la Escuela de Medicina de la Universidad de Puerto Rico, se llevará a cabo en el Hotel Dorado Beach los días 5 y 6 de septiembre de 1982.

Serán dos días de actualización en cardiología durante los cuales se discutirán los siguientes tópicos: Fallo Cardíaco/ Nuevos Avances Diagnósticos en Enfermedades Cardiovasculares incluyendo Cardiología Pediátrica/ Arritmias/ Marcapasos/ y Cirugía Vascular

Compartirán con nosotros figuras tales como:
Carlos de Castro, Houston, Texas
Peter Gazes, Charleston, South Carolina
Thomas P. Graham, Nashville, Tennessee
Jay W. Harthorne, Boston, Massachusetts
Julio E. Pérez, Saint Louis, Missouri
Jesse E. Thompson, Dallas, Texas

Los asistentes al curso recibirán doce (12) horas-crédito en Categoría I.

Próximamente se le enviará el programa, blancos de matrícula y registro del hotel.

Para mayor información puede comunicarse con la Asociación Puertorriqueña del Corazón: 763-8275, 751-6595 y 759-8410 ó con la División de Educación Médica Continuada de la Escuela de Medicina.

M. Etienne Otaño, M.D.
Presidente
Asociación Puertorriqueña del Corazón

Carlos E. Girod, M.D.
Presidente
Comité de Asamblea Anual

CARDIO 82
Asociación Puertorriqueña del Corazón

ABSTRACTOS SESION CIENTIFICA

El Comité de Asamblea invita a enviar abstractos de trabajo originales para considerarse para presentación durante la sesión científica. Cardio-82, que se llevará a cabo los días 5 y 6 de septiembre de 1982, en el Dorado Beach Hotel.

Procedimientos:

1. Enviar un abstracto de 250 palabras o menos en maquinilla a doble espacio. Se necesitarán original y tres copias. El abstracto debe llenar los siguientes requisitos:

    a. Título
    b. Autores
    c. Institución
    d. Introducción y propósito
    e. Métodos
    f. Resultados
    g. Conclusión

2. Adjuntar en una tarjeta 3 x 5 con los siguientes datos, en el siguiente órden:

    a. Autor principal - dirección y teléfono.
    b. Autor que hará la presentación.
    c. Autores colaboradores.
    d. Título del trabajo.
    e. Institución del estudio, ciudad.
    f. Equipo audiovisual que se requiera para la presentación.

3. Enviar lo anterior antes de julio 15 a:

    Dr. Etienne Otaño
    Presidente
    Asociación Puertorriqueña del Corazón
    Apartado 1752
    Hato Rey, Puerto Rico 00919

ASOCIACION MEDICA DE PUERTO RICO

BOLETIN

INSTRUCCIONES PARA LOS AUTORES

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

Se urge a los autores se esfuerzen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos no importa el tema o formato del manuscrito.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito

El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquinilla a doble espacio; por un solo lado de cada página, en TRIPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

Nomenclatura

Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

Tablas

Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al mejor entendimiento del manuscrito.

Ilustraciones

Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor. Debe indicarse en la parte superior de la ilustración.

Resumen

Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

Referencias

Las referencias deben ser numeradas sucesivamente de acuerdo a su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Deben utilizarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana. Las referencias deben seguir el patrón que se describe a continuación.

1. Para artículos de revistas: *Apellido(s) e iniciales del nombre del autor(es), título del artículo, nombre de la revista, año volumen, número, páginas. Por ejemplo:*
   Villavicencio R: Soplos Inocentes en Pediatría. Bol. Asoc. Med. PR 1981; 73 (10): 479-87
   Si hay más de 5 autores, incluir los primeros 3 y añadir et al.
2. Para citación de libros donde el autor(es) del capítulo citado es a su vez el (los) editor(es): *Apellido(s) e iniciales del autor(es), título del libro, número de edición, ciudad, casa editora, año y página, Por ejemplo:*
   Keith JD, Rowe RD, Vlad P: Heart Disease in Infancy and Childhood, 3d. Ed., New York, MacMillan, 1978, p. 789
3. Para citación de libros donde el editor(es) no es el autor(es) del capítulo citado se añade el autor(es) del capítulo y el título del mismo. Por ejemplo:
   Olley PM: Cardiac Arrythmias: In: Keith JD, Rowe RD, Vlad P Eds. Heart Disease in Infancy and Childhood. 3d Ed., New York, MacMIllan, 1978, p 275-301
   Observar que no se usa el punto después de las iniciales de los autores ni al final de las referencias.

Cartas al Editor

Se publicarán a discreción de la Junta Editora. Deben estar escritas en maquinilla a doble espacio, no deben ser mayor de 500 palabras, ni incluir más de cinco referencias.

INSTRUCTIONS TO AUTHORS

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

All authors are urged to seek clarity, brevity, and pertinence in the manuscripts regardless of subject or format.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts

The entire manuscript, including legends and references should be typewritten double spaced in TRIPLICATE with ample margins. A separate title page should include the following: title, authors and their degrees (e.g. MD, FACP),city where the work was done, hospital or academic institutions, acknowledgement of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Nomenclature

Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurement should be used preferentially).

Tables

These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted. The language used in the tables must be the same as that of the article. Include only those tables which will enhance the understanding of the article. They should supplement, not duplicate the text.

Figures

Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

Summary

An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

References

These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text.

1. For periodicals: *Surname and initials of author(s), title of article, name of journal, year, volume, pages. For example:*
   Villavicencio R.: Soplos Inocentes en Pediatría. Bol Asoc Med PR 1981; 73 (10): 479-87
   If there are more than 5 authors list only 3 and add et al.
2. For books when the author of the cited chapter is at the same time the editor: *Surname and initials of author(s), title, edition, city, publishing house, year and page. For example:*
   Keith JD, Rowe RD, Vlad P: Heart Disease in Infancy and Childhood, 3d Ed., New York. MacMillan. 1978. p 789
3. For chapter in book when the author of the chapter is not one of the editors: *Olley PM: Cardiac Arrythmias. IN: Keith JD, Rowe RD, Vlad P. Heart Disease in Infancy and Childhood, 3d Ed, New York, MacMillan, 1978, 275-301*

   Please note that the period is ommitted after the author's initials and at the end of the references.

Letters to the Editor

Will be published at the discretion of the Editorial Board. They should be typewritten double-spaced, should not exceed 500 words nor more than five references.

FUNDADO EN 1903

ASOCIACION MEDICA DE PUERTO RICO

BOLETIN

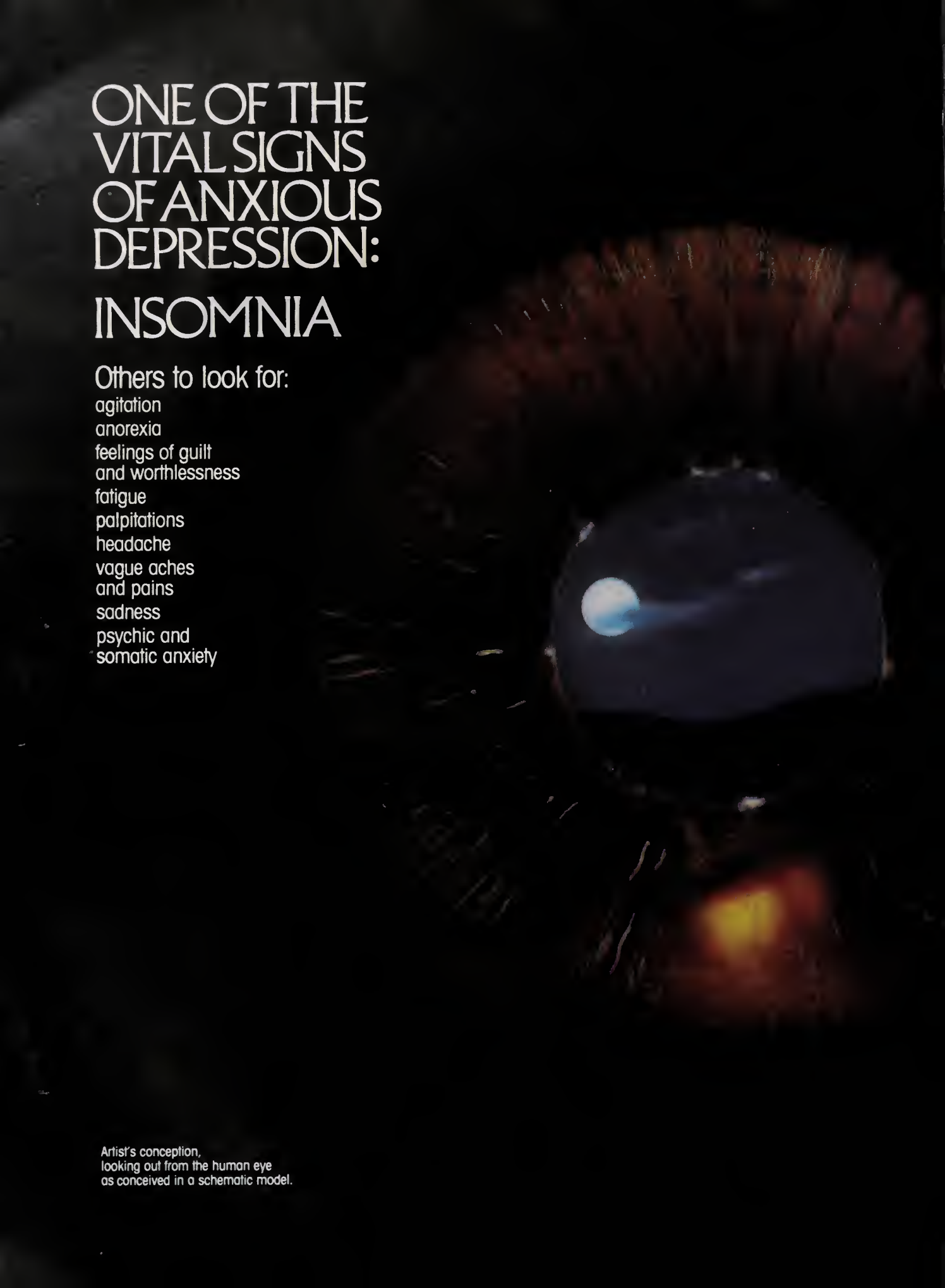
VOL. 74/NUM. 4 ABRIL 1982

ONE OF THE VITAL SIGNS OF ANXIOUS DEPRESSION:

INSOMNIA

Others to look for:

agitation
anorexia
feelings of guilt and worthlessness
fatigue
palpitations
headache
vague aches and pains
sadness
psychic and somatic anxiety



Artist's conception,
looking out from the human eye
as conceived in a schematic model.

ROCHE

LIMBITROL GIVEN H.S.: ONE OF THE VITAL SPECIFICS OF TREATMENT

Limbitrol brings a special—and specific—quality of relief to most anxious depressed patients. Insomnia, for example, responds with particular promptness. Other symptoms likely to respond within the first week of treatment include anorexia, agitation and psychic and somatic anxiety. And, as the depression and anxiety are alleviated, in many cases so are such related somatic symptoms as headache, palpitations, and various vague aches and pains.

Limbitrol given once daily h.s. may be the best approach

Many patients respond readily to a single bedtime dose of Limbitrol, a convenient schedule that may enhance compliance and helps relieve the insomnia associated with anxious depression. Limbitrol also offers a choice of other regimens: t.i.d., or a divided dose with the larger portion h.s. In all cases, caution patients about the combined effects with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as driving or operating machinery.

in moderate depression and anxiety

Limbitrol® IV

Tablets 5-12.5 each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt)
Tablets 10-25 each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt)

Specific therapy with h.s. dosage convenience

Please see summary of complete product information on following page.

LIMBITROL® TABLETS Tranquilizer—Antidepressant
Before prescribing, please consult complete product information, a summary of which follows:
Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.
Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.
Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving).
***Usage in Pregnancy:* Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**
Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).
Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. Concomitant use with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.
Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.
The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:
Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.
Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.
Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.
Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.
Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.
Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.
Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.
Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female and elevation and lowering of blood sugar levels.
Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.
Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.
Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly.
Limbitrol 10-25, initial dosage of three to four tablets daily in divided doses, increased to six tablets or decreased to two tablets daily as required.
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COLUMNA DEL EDITOR

En este número incluimos otra nueva sección, la hemos titulado *Medicina al Día.* En ella aparecerán diferentes temas los cuales serán desarrollados por expertos en los mismos. De esta forma pretendemos conseguir una exposición completa, y actualizada del material discutido, lo cual será sin duda de un gran provecho práctico y académico para nuestros lectores. El primer tema de esta sección: "Reflujo Gastroesofágico en Pediatría" es sumamente importante, de gran significado clínico y de una incidencia mucho mayor que la sospechada hasta el presente.

Reaparecen los *Artículos Especiales,* de interés y contenido variable, no necesariamente clínicos, pero de valor científico indudable. Muchas veces tratarán sobre aspectos éticos, médico-legales, o filosóficos de la Medicina.

Estas nuevas secciones probablemente no sean fijas en cada número, pues dependerá del material que recibamos de nuestros colaboradores, algo que con el nuevo formato y mejoramiento de la revista esperamos incremente su motivación a hacerlo. A su vez, estas nuevas secciones proveen medios para ampliar el espectro del contenido del Boletín.

Además de lo anterior me satisface comunicarles que contamos con un nuevo Director del Boletín. En la última reunión de la Junta de Directores de la Asociación Médica se aprobó de forma unánime que el Señor José R. Villavicencio pasase a asumir dicha posición con carácter de empleado permanente de la Asociación Médica de Puerto Rico. Se reconoció su labor en la transformación del Boletín y se admitió que la única forma en que nuestro órgano oficial podía dejar de ser un lastre económico y convertirse en una publicación autosuficiente y digna de nuestra clase médica era encargarlo a un profesional en este campo, y que el Sr. Villavicencio había de sobras demostrado su capacidad e interés para lograrlo. Su posición incluye también asesoramiento y supervisión de los servicios gráficos y de imprenta de la Asociación. La Junta de Directores le confirió a este cargo la autoridad necesaria para poder ejercer sus funciones a plena capacidad para asegurar el logro de los objetivos señalados. El Sr. Villavicencio trabajará en estrecho contacto y canalizará sus responsabilidades directamente al *Comité del Boletín,* el cual está compuesto por el Presidente, el Tesorero, y el Secretario de la Asociación Médica junto con el Presidente del Comité de Finanzas y el de la Junta Editora.

Estimo que la decisión de crear dicho puesto producirá beneficios de toda índole a nuestra Asociación. El Director del Boletín ha propuesto ideas y proyectos a corto y largo plazo que consideramos excelentes y creemos que conducirán al logro de nuestra meta en un tiempo razonable.

Le damos la bienvenida al Sr. Villavicencio a la familia de la Asociación Médica de Puerto Rico. Hemos depositado en él nuestra confianza y le debemos todo nuestro apoyo. Le deseamos éxito en esta difícil empresa, pues su éxito será también el de la Asociación Médica de Puerto Rico y todo lo que ella representa.

RAfael Villavicencio M.D.
Presidente, Junta Editora
Boletín Asociación Médica de
Puerto Rico

NUESTRA PORTADA:

"Los Chiringueros" óleo del pintor puertorriqueño Wichie Torres, y uno de los temas favoritos del artista. La obra que ocupa nuestra portada fue uno de los varios trabajos sobre las chiringas que él ofreció para la producción de un cartel conmemorando el Festival de la Chiringa y el Tiguero de 1982 celebrado en el pueblo de Lajas.

Wichie Torres nació en Ponce en marzo de 1952 donde recibió sus primeras instrucciones de pintura con la profesora Carola Colom Covas. Luego realiza estudios adicionales en la Escuela de Artes Plásticas del Instituto de Cultura Puertorriqueño en el verano de 1968. Al año siguiente se traslada a Nueva York, toma lecciones con el profesor Rafael López Sustachi, y durante un certamen de pintura auspiciado por la Universidad Católica de Puerto Rico obtiene una beca que le garantiza sus estudios. Esto lo trae de regreso a su ciudad natal donde permanece hasta 1973. En ese año se desplaza a Ciudad de México donde se radica por año y medio, absorbiendo en esa ciudad técnica, colorido y temas. Para 1975 regresa a la isla y continúa su quehacer artístico con su característico estilo e incansable vigor que lo convierten en corto tiempo en uno de los grandes valores de las artes plásticas nacionales.

Además de las principales galerías de arte del país, Wichie ha expuesto sus obras en instituciones de comprobado prestigio cultural como: el Museo de Arte de Ponce, la Universidad Católica de Puerto Rico, el Colegio de Agricultura y Artes Mecánicas de Mayagüez, la Universidad de Puerto Rico, la Universidad Interamericana, el Palacio de Santa Catalina y las Alcaldías de San Juan y Ponce. En el extranjero sus obras han figurado en exposiciones en la Universidad de San Marcos (Perú) la Galería Anhers (Venezuela), Spanish American Cultural Center (Wisconsin), en exposiciones colectivas en Ciudad de México, Washington D.C. y Nueva York. Cabe destacar la colaboración continua de nuestro artista con la Casa del Médico en Ponce donde viene celebrando exposiciones desde 1973.

Sus temas lo constituyen estampas del diario vivir de nuestro pueblo, sus tradiciones y sus costumbres. "Los Chiringueros" es un vivo ejemplo de ello, quedando magistralmente plasmado por el autor.

La reproducción de "Los Chiringueros" en nuestra portada ha sido una cortesía hacia la Asociación Médica de Puerto Rico del autor y del Taller-Galería André en el Condominio El Centro de Hato Rey, donde se encuentra expuesta la obra.

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	Whipworm	Common Roundworm	Hookworm	Pinworm
cure rates				
mean	68%	98%	96%	95%
(range)	(61-75%)	(91-100%)	—	(90-100%)
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mean	93%	99.7%	99.9%	—
(range)	(70-99%)	(99.5%-100%)	—	—

CONTRAINDICATIONS VERMOX is contraindicated in pregnant women (see Pregnancy Precautions) and in persons who have shown hypersensitivity to the drug.

PRECAUTIONS *PREGNANCY:* VERMOX has shown embryotoxic and teratogenic activity in pregnant rats at single oral doses as low as 10 mg/kg. Since VERMOX may have a risk of producing fetal damage if administered during pregnancy, it is contraindicated in pregnant women.

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DOSAGE AND ADMINISTRATION The same dosage schedule applies to children and adults. The tablet may be chewed, swallowed or crushed and mixed with food. For the control of pinworm (enterobiasis), a single tablet is administered orally, one time. For the control of common roundworm (ascariasis), whipworm (trichuriasis), and hookworm infection, one tablet of VERMOX is administered, orally, morning and evening, on three consecutive days. If the patient is not cured three weeks after treatment, a second course of treatment is advised. No special procedures, such as fasting or purging, are required.

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CONTENIDO

EDITORIAL

El Tratamiento del Paciente Asmático

Nuestra intención al comentar el artículo que aparece en este número del boletín sobre "El Tratamiento del Niño Asmático en el Hospital" no es diseñarle al lector un método para tratar el asma bronquial, pues eso se conoce y en la literatura hay ejemplos magníficos de ello.[1,2] Nuestro afán es el mencionar situaciones y factores que a veces pasan desapercibidos en el tratamiento del asma y que se han demostrado son muy importantes para el éxito final de nuestra misión como médicos responsables de tratar a pacientes con asma bronquial.

No sabemos con certeza toda la fisiopatología del asma bronquial pero los conocimientos que tenemos son suficientes para que aplicados de una manera ordenada y sistemática podamos aliviar a la mayoría de los pacientes con asma.

El desconocimiento de la totalidad de esa fisiopatología ha sido la causa de que el tratamiento del asma bronquial ha sido muchas veces expresiones subjetivas e improvisaciones de parte de médicos y pacientes en un afán inútil de encontrar esa "cura total" que todos deseamos pero que todavía nos rehuye.

La importancia del artículo del Dr. Sifontes reside en que ofrece una alternativa sistemática para todo aquel que tenga la responsabilidad de cuidar al niño asmático en el ambiente hospitalario. Para aquellos que tienen la responsabilidad de cuidar el asmático adulto la importancia de tener un sistema de tratamiento es todavía más importante, pues el asmático adulto lo más probable es que concomitantemente con el asma padezca de otras condiciones nosológicas que lo hagan un paciente más susceptible a complicaciones y la mortalidad en el adulto con "status asthmaticus" es más alta que en el niño.

La obesidad y el asma bronquial son dos condiciones en que dependiendo de la manera en que el médico y el paciente se enfrenten a ella pueden ser causa de grandes satisfacciones o por el contrario son gran fuente de frustraciones y desencantos.

Ambas necesitan de una actitud bien informada y positiva y ambas necesitan de una investigación detallada en cada paciente de todos los factores que las perpetuan, las precipitan o las mejoran. Si para el paciente asmático es motivo de frustraciones al verse objeto de muy pocas atenciones cuando se halla en salas de emergencias o en un hospital, también para el médico resulta frustrante el ver repetidas veces al mismo paciente asmático sin aparente alivio, hospitalizarse una y otra vez o visitar de forma repetitiva la sala de emergencia con angustia respiratoria.

Algo hemos podido adelantar en los últimos años para disminuir o evitar estas frustraciones repetidas que sufren pacientes asmáticos y los médicos que los tratan. Sabemos, que el mejor tratamiento del "status asthmaticus" es el evitarlo y con un tratamiento cuidadoso podemos hacerlo en la mayoría de las ocasiones.

Sabemos que la causa más frecuente de fallas en el tratamiento del asmático es el tratamiento insuficiente, ya sea porque no ingiere la medicación en forma y cantidad adecuada y que la medicación apropiada no le ha sido prescrita correctamente. La comunicación entre paciente asmático y su médico debe de estar abierta a consulta constantemente.

Sabemos que la mayoría de los pacientes que tienen asma no conocen claramente la naturaleza de su condición. Debe de comprender la necesidad de ingerir su medicación de una manera sistemática y no de una manera sintomática como la mayoría de los pacientes y médicos por muchos años lo han considerado.

El tratamiento del asma debe de ser algo continuo como el de la hipertensión o la diabetes mellitus. Es un desequilibrio del paciente frente a su medio ambiente; desequilibrio que hay que mantener restablecido mediante la ingestión de la combinación de broncodilatadores que el médico haya estimado como el más apropiado para cada paciente en particular. El asmático no debe tratarse con "cocktails" o regímenes pre-establecidos. Hay que individualizar el tratamiento y para eso existen una pléyade de medicamentos broncodilatadores de los cuales el clínico debe de escoger la combinación más adecuada con el menor número de efectos secundarios para cada paciente. A veces hay que tratar con diferentes tipos y dosificaciones y luego de determinaciones sanguíneas de los niveles llegar a la cantidad y a la frecuencia que mantengan al paciente lo más cumplidor posible con el régimen prescrito específicamente a sus necesidades.

Sabemos, que el uso de las combinacions de broncodilatadores funcionan mejor que el uso de un solo tipo de broncodilatador. Es mejor combinar una teofilina y una agonista Beta 2 que cualquiera de ellas individualmente; a veces a la combinación de teofilina y agonistas hay que añadir esteroides orales en las dosis menores posibles para

mantener a un paciente fuera de peligro de sufrir repeticiones de "status asthmaticus" con el consiguiente aumento en la morbilidad y la mortalidad de la condición.

Sabemos, que la mortalidad de el asma ocurre más frecuentemente en pacientes que han estado automedicándose porque se han sentido frustrados con los tratamientos de múltiples médicos en múltiples sitios y usualmente o usan atomizadores de broncodilatadores o se compran equipos de terapia respiratoria para el uso y mal uso en sus hogares con el consabido aumento de arritmia cardiácas, infecciones, broncoespasmos y muertes súbitas.

Tenemos que evitar que estas frustraciones aumenten más allá de lo que ya han ocurrido y esto solamente lo podemos conseguir mediante la educación del paciente sobre su condición y el no alentar esperanzas falsas de curación total, pero tampoco transmitir pesimismo y frustraciones. El asmático y el obeso son las presas más fáciles de los charlatanes que ofrecen curas milagrosas y esto lo tenemos que evitar a través de la educación de los pacientes y sus familiares.

En años recientes hemos aprendido que hay factores ambientales que son precipitantes del broncoespasmo. Los conceptos de asma "inducido por el ejercicio", "asma emocional" y asma por "humedad o frío"[3 4 5 6] sabemos que son debidos a alteraciones en la humedad y la temperatura de la mucosa bronquial y que estos cambios son más determinantes que la liberación de los mediadores bioquímicos conocidos por nosotros desde hace más tiempo y que creíamos eran los únicos responsables del broncoespasmo.

Sabemos, que tanto en países templados como en países tropicales la mucosa de los bronquios puede ser afectada por cambios ambientales de temperatura y humedad que pueden provocar el broncoespasmo. En la práctica médica el interrogatorio del paciente asmático con respecto a la relación entre síntomas y condiciones ambientales, actividades diarias y situaciones vivienciales pueden sugerirle al médico si estos factores son importantes en cada caso en particular.

Sabemos que hay pacientes con tanta frustración y ansiedad por su condición asmática que pequeñas dosis de ansiolítico están perfectamente indicados a su tratamiento ambulatorio y en el hospitalario siempre que se pueda en el hospital tener el beneficio de la determinación de los gases arteriales para evitar situaciones potencialmente mortales.

Sabemos en resumen, que aunque el paciente asmático es un paciente para toda la vida, puede disfrutar de una vida plena y feliz si se educa apropiadamente, se evalúa con todo el detenimiento y rigor que una condición potencialmente mortal lo amerita y se medica con una combinación o combinaciones de medicamentos especialmente prescritos para cada paciente individual y tomando en cuenta factores ambientales, sicológicos y sociales que antes no eran tomados en cuenta. Sólo así podremos ayudar a la gran porción de nuestra población que padece de asma bronquial.

Ramón E. Figueroa Lebrón, MD, FCCP
Presidente, Sección Neumología
Asociación Médica de Puerto Rico
Regent, American College of Chest Physicians

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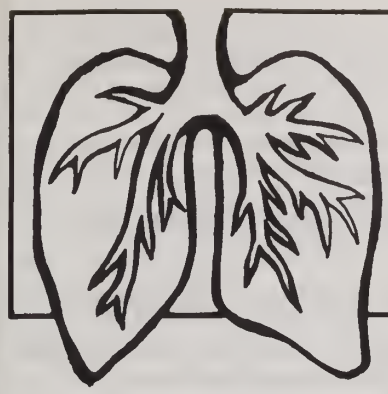

ESTUDIOS CLINICOS

Tratamiento del Niño Asmático en el Hospital

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Resumen: El paciente asmático que llega a la sala de emergencia del el hospital debe atenderse y evaluarse inmediatamente. Se sugiere el siguiente esquema de manejo: (1) Historia y exploración clínica rápidamente y dirigidas a lo pertinente. (2) Separar con prontitud los que pueden tratarse inicialmente en la sala de emergencia de los que necesitan hospitalización. (3) Epinefrina subcutanea y aerosolterapia con los agonistas beta 2 (si están disponibles), (4) Si no hay mejoría notable y pronta, aminofilina por la vía endovenosa. (5) Oxigenoterapia. (6) Hidratación adecuada pero no excesiva. (7) Corticosteroides a tiempo —no debe esperarse que el paciente se deteriore. (8) Establecer tablas o gráficas de seguimiento en las que se anoten a intervalos de 1/2, 1, 2, ó 3 horas, según sea necesario (véase tabla 9): (a) la puntuación clínica, (b) las cifras del pico del flujo espiratorio o espirometría (si están disponibles), (c) frecuencias cardíaca y respiratoria y presión arterial, (d) las cifras de gases arteriales, si se miden, (e) las cifras de teofilina sanguínea, si se miden. (9) Pruebas de laboratorio según estén indicadas: (a) radiografías de tórax, (b) hemograma incluyendo hematocrito, (c) urinálisis incluyendo peso específico, (d) coproparasitología, (e) prueba de la tuberculina, (f) mediciones de los gases arteriales y electrolitos séricos. (10) Si el paciente necesita hospitalizarse debe ser en la unidad de cuidado intensivo o especial o en donde pueda ser vigilado continuamente hasta que su condición se estabilice.

El ataque agudo del asma bronquial es una urgencia pediátrica. Se define como la crisis de disnea espiratoria con sibilancias difusamente repartidas en ambos campos pulmonares.[1] El ataque puede ser el primero o uno de muchos. Su substrato fisiopatológico es el espasmo bronquial generalizado y reversible, el edema de la mucosa y la hipersecreción de moco por las glándulas bronquiales. Estos trastornos se traducen en prolongación de la fase espiratoria, el atrapamiento de aire y la hipoventilación alveolar. Cuando el enfermo empeora a pesar del tratamiento adecuado entra en la fase del estado asmático ("status asthmaticus"). Esta es la condición en la que hay una probabilidad significativa de que la insuficiencia respiratoria vaya a suceder si no se ofrece un tratamiento pronto y enérgico.[2] El ataque agudo de asma bronquial plantea un diagnóstico diferencial con diversas afecciones tales como cuerpos extraños, bronquiolitis, bronconeumonía y otras cuyo diagnóstico se supone haya sido establecido al fijar las pautas terapéuticas señaladas en este trabajo. En el mismo se actualizan y se amplían las ya fijadas en el 1970.[1]

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TABLA I

Evaluación Inicial del Niño Asmático en la Sala de Emergencias

Historial

1. Medicamentos: preparados, dosis, frecuencia, alergia, intolerancia.
2. Duración del acceso agudo: fecha y hora del comienzo, factor precipitante
3. Pérdidas de líquidos y electrolitos: ingesta, vómitos, diarrea.
4. Antecedentes: respuesta a los tratamientos previos, admisiones previas al hospital
5. Infección, fiebre, faringalgia, otalgia, secreciones purulentas

Exploración Física

1. Aspecto general; alerta, obnubilado
2. Hidratación
3. Valoración clínica (véase la tabla 3)
4. Pulso paradójico*

Laboratorio

1. Hematocrito
2. Peso específico de la orina

* El pulso paradójico se produce por la disminución de la presión arterial en la inspiración. En los niños se determina por medición de:

a. Cifra de presión sistólica inicial cuando aparecen los primeros ruidos de Korotkoff de intensidad regular.
b. Cifra más alta de la presión sistólica cuando los ruidos de Korotkoff empiezan a disminuir en intensidad y se tornan irregulares.
A - B = Pulso paradójico (P.P.)
Ejemplo: si A = 120 mmHg y B = 100 mmHg, PP = mmHg
Referencia: (3)
c. En los niños mayores que pueden cooperar, el pulso paradójico se mide a base de la diferencia entre la presión sistólica en inspiración y espiración.

El tratamiento del asma bronquial ha de estar dirigido primordialmente a la prevención del acceso, a mantener el enfermo libre de síntomas y permitirle llevar una vida normal. Los medios de lograr estos objetivos se presentaron en un artículo reciente.[2] Pero en muchos casos, quizás demasiados, el tratamiento ambulatorio fracasa. Las causas comunes de este fracaso comprenden entre otras: (a) las dosis de los medicamentos son insuficientes, (b) los mismos no se emplean a tiempo y a intervalos adecuados, (c) infecciones respiratorias agudas, (d) atelectasias, (e) bronconeumonía, (f) neumotórax y neumomediastino, (g) deshidratación, (h) exposición persistente y excesiva a los alergenos o agentes que precipitan el asma (cemento, polvo, animales, olores fuertes, cigarillos, aire contaminado, aspirina, etc., (i) ansiedad excesiva conducente a estado de pánico en el paciente y sus familiares, (j) factores socioeconómicos que impiden modificar el ambiente o el cumplimiento con el plan de tratamiento prescrito. Cuando el tratamiento ambulatorio fracasa es necesario que el paciente acuda a la sala de emergencias del hospital para tratamiento de urgencia y, si es necesaria, la hospitalización. El propósito de este trabajo es describir el manejo del asmático que llega al hospital.

En el mismo se describen métodos que todavía no se han adoptado en nuestros servicios pediátricos pero que deben ser conocidos y utilizados en la medida que esto sea posible de acuerdo con los recursos disponibles. Por ejemplo, la medición del pico del flujo espiratorio, el tratamiento con isoproterenol por la vía endovenosa y la medición de las cifras sanguíneas de teofilina.

Evaluación Inicial

El paciente que acude a la sala de emergencias con un acceso asmático plantea una serie de importantes decisiones al facultativo que lo recibe. Primeramente hay que decidir sin demora si el enfermo debe admitirse inmediatamente para cuidado intensivo o si se puede tratar inicialmente en la sala de emergencias. Esto se debe hacer mediante la historia y examen físico incluyendo en aquélla los datos pertinentes al problema inmediato (Tabla I). No es este el momento para recoger una gran cantidad de datos, posiblemente interesantes, pero que no ayudan a resolver el problema inmediato y mientras tanto se pierde tiempo precioso que podría emplearse en comenzar un tratamiento potencialmente crucial para evitar el deterioro del enfermo. El paciente con asma de mayor severidad que se va a hospitalizar debe evaluarse más cuidadosamente (Tabla 2). Pero siempre teniendo en cuenta que este no es el momento para mandar un paciente con dificultad respiratoria, que probablemente necesita oxigenoterapia, a trasladarse de un sitio a otro ya sea para papeleos o pruebas de laboratorio; todos estos deben venir al paciente y no el paciente hacia ellos. Es en este momento que se deben hacer las decisiones de comenzar oxigenoterapia, administrar líquidos y medicamentos endovenosos, inyectar epinefrina y administrar aerosolterapia con broncodilatadores. Y las decisiones deben estar seguidas de acciones inmediatas.

El objetivo de hospitalizar el enfermo es obtener la mejoría lo más rápidamente posible, evitar la insuficiencia respiratoria y tratar esta adecuadamente si es que sucede. Es importante recoger y anotar desde la llegada del enfermo los datos sobre los signos vitales, los gases arteriales y la valoración clínica con la frecuencia que sea necesaria. Estos deben aparecer en el expediente en forma clara ya sea por medio de tablas o de gráficas.

Tabla II

Evaluación Inicial del Asmático Hospitalizado

Radiografía de Tórax
Medición de pO_2, pCO_2 y pH arteriales y electrolitos séricos
Medición del pico del flujo espiratorio o espirometría incluyendo respuesta a los broncodilatadores
Signos vitales incluyendo pulso paradójico
Electrocardiograma
Medición de entrada y salida de líquidos
Cultivo de sangre si hay indicaciones
Hemograma y hematocrito, coproparasitología
Urinálisis incluyendo medición del peso específico y pH
Prueba de la tuberculina

Decisión de Hospitalización

Las indicaciones para hospitalización en los casos graves están claramente establecidas. Las más comunes se enumeran en la Tabla 3. En los casos menos severos la decisión puede que dependa de la calidad del hogar del enfermo o de la accesibilidad que este tenga al hospital. En los pacientes con dificultad respiratoria que va en aumento, a pesar del tratamiento aparentemente adecuado, no hay lugar a dudas sobre la necesidad de la hospitalización. Puede estar indicada también por vómitos, neumonía, atelectasia y otras complicaciones. En estos casos la decisión dependerá de la severiedad de la complicación, de la magnitud de las alteraciones d ela función pulmonar, de la calidad del hogar del enfermo y de las limitaciones para el seguimiento ambulatorio cuidadoso.

TABLA III

Indicaciones Comunes para la Hospitalización del Niño Asmático

- Las sibilancias persisten y no hay mejoría al cabo de 2 horas en la sala de emergencias
- Evidencia de que no hay mejoría o de deterioro por
  - las pruebas de función pulmonar o
  - puntuación clínica (véase la fig. 1)
- Signos de insuficiencia respiratoria (véase la tabla 4)
- Antecedentes de problemas conducentes a la hospitalización
- Complicaciones tales como
  - neumonía
  - neumotórax, neumomediastino, enfisema subcutaneo
  - deshidratación y trastornos hidroelectrolíticos
  - atelectasia

Los pacientes que muestran ansiedad y agitación que va en aumento o que están obnubilados deben admitirse al hospital sin demora. Igualmente los que manifiestan dificultad respiratoria que va en aumento y repentinamente parecen aliviarse, abandonan los esfuerzos respiratorios y entran en un estado de estupor. Estos y otros signos de insuficiencia respiratoria son indicaciones claras para la hospitalización inmediata. Es esencial conocer e identificiar sin demora los signos y síntomas de la insuficiencia respiratoria. Estos se resumen en la tabla 4 y en las figuras 1 y 2 donde se presenta un plan de acción acompañado de un sistema de valoración que permite identificar la insuficiencia respiratiria. La inatención a las manifestaciones de ésta es probablemente la causa principal de muertes por asma bronquial. Un paciente con gran dificultad respiratoria no debe mantenerse horas y horas en la sala de emergencias para ver si con el suero de aminofilina no desarrolla insuficiencia respiratoria. Este enfermo puede entrar abruptamente en fallo cardiorespiratorio y morir antes de que se le puedan prestar las medidas de reanimación.

TABLA IV

Señales de Insuficiencia Respiratoria en el Asma Bronquial

- Ansiedad
- Obnubilación
- Conducta sicótica
- Confusión
- Trastorno de la visión
- Cianosis
- Retracciones intensas
- Ausencia de ruidos repiratorios
- Pulso paradójico sobre 20 mmHG

Los pacientes que después de una rápida evaluación inicial demuestran dificultad respiratoria leve o moderada pueden ser atendidos inicialmente en la sala de emergencias. El problema es identificar tempranamente cuales de éstos necesitarán hospitalización y cuáles podrán continuar en tratamiento ambulatorio después de estabilizarse su condición en la sala de emergencias. Signos favorables son cifras bajas de la valoración clínica (figura 1) y la ausencia de pulso paradójico (PP) o cifras de PP menores de 12 mmHg.[3]

La respuesta inicial a la epinefrina y las cifras del pico de flujo espiratorio del paciente permiten identificar los pacientes que tienen mayores probabilidades de necesitar hospitalización o de regresar dentro de 48 horas después del tratamiento inicial[4]. La medición del pico del flujo espiratorio es un método sencillo que puede llevarse a cabo en los mayores de 5 años empleando equipo de bajo costo y portátil ("Mini Wright Peak Flow Meter", Armstrong Industries, Inc., P.O. Box 7, Northbrook, Illinois 60062 - alrededor de $60.). Los resultados de estas mediciones identifican los enfermos que probablemente necesitarán hospitalización. Los criterios son los siguientes: (a) Si el pico del flujo espiratorio antes del tratamiento inicial es de 10% o menos de lo esperado. (b) Ausencia de respuesta a las inyecciones de epinefrina o respuesta parcialmente solamente. Si después de la primera inyección el pico del flujo espiratorio continúa por debajo del 40% de lo esperado es probable que el enfermo necesitará hospitalización. (c) Si después de una mejoría inicial aparecen nuevamente los signos de asma y el pico del flujo espiratorio disminuye 15% o más es probable que persistirá el deterioro y que la hospitalización será necesaria. (d) Los pacientes que se dan de alta de la sala de emergencia con cifras del pico de flujo espiratorio menores de 64% de lo esperado es probable que regresen dentro de 48 horas con manifestaciones recurrentes. La mejor base para determinar el pico del flujo espiratorio "esperado" es el mismo paciente. Por esta razón, es aconsejable la medición del pico del flujo espiratorio periódicamente cuando estos pacientes están libres de los accesos asmáticos.

FIGURA I

Valoración Clínica de Asma
(Clinical Asthma Evaluation Score)
— Modificada de Wood et al. —*

Observaciones	Puntuación 0	1	2
PO_2 arterial mm. de Hg	70-100 respirando aire	Menos de 71 respirando aire	Menos de 71 respirando oxígeno 40%
Cianosis	No	Cianosis respirando aire	Cianosis respirando, oxígeno al 40%
Ruidos inspiratorios	Normales	Desiguales	Disminuido o Ausentes
Músculos accesorios	No se utilizan	Moderado esfuerzo	Máximo esfuerzo
Sibilancias Espiratorias	Ausentes	Moderadas	Marcadas
Función Cerebral	Normal	Deprimido o agitado	Coma

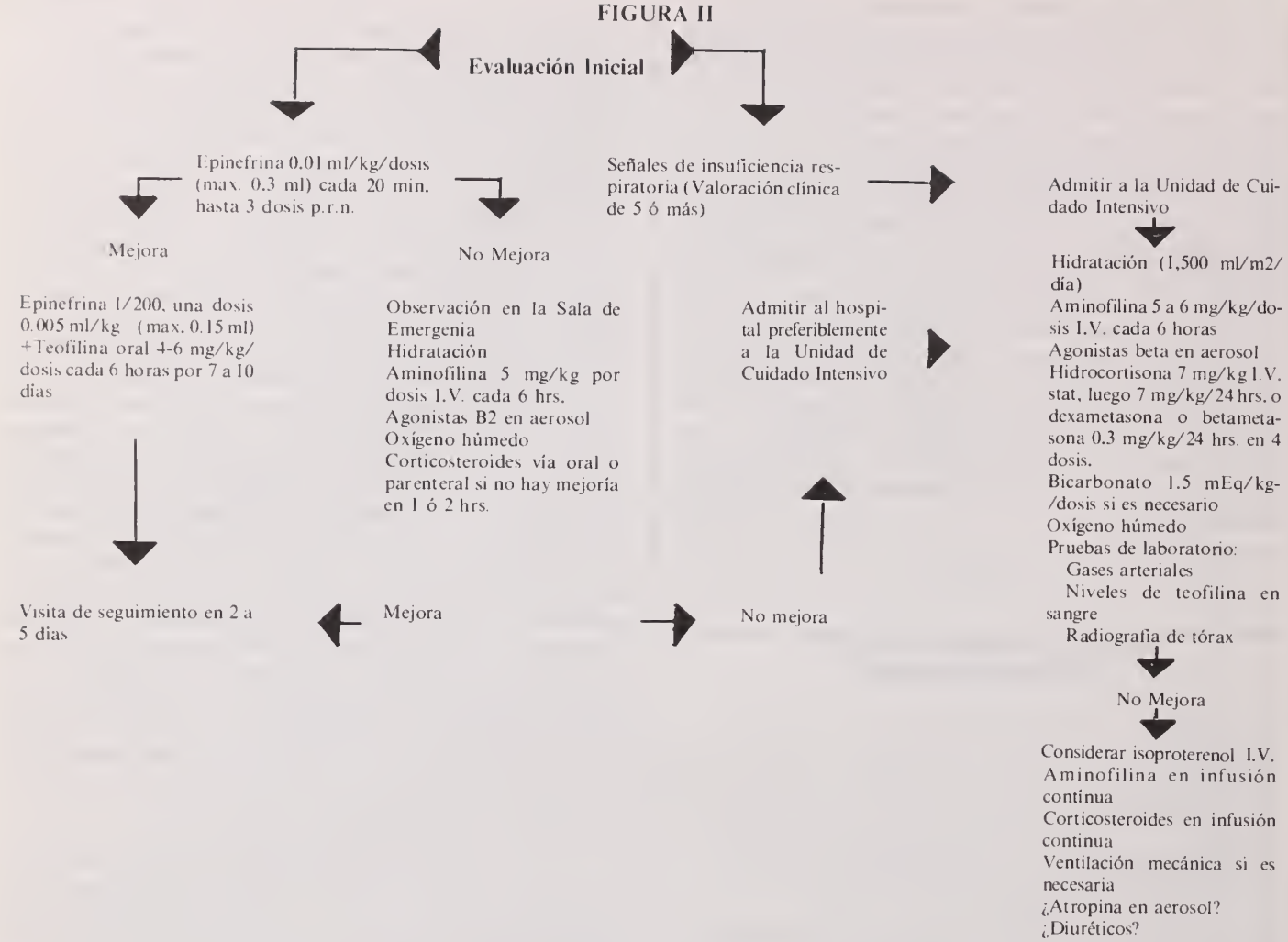
Significado:

5 ó más: = inminente fallo respiratorio

7 ó más: = fallo respiratorio

* Am J Dis Child 120:227, 1972.

FIGURA II



La conducta a seguir después de la respuesta al tratamiento inicial o de la evaluación preliminar al llegar el enfermo a la sala de emergencias debe ajustarse a las necesidades individuales. Las recomendaciones que se hacen a continuación y que se resumen en la figura 2 señalan unas pautas generales pero no deben considerarse como trayectorias, rígidas y inviolables.

Farmacoterapia

Agonistas beta. El primer medicamento que se le administra al asmático es la epinefrina (si es que no la ha recibido pocas horas antes). Se administra por la vía subcutanea en dosis de 0.01 mg/kg de peso hasta un máximo de 0.3 ml. La inyección se puede repertir hasta 2 veces a intervalos de 20 minutos. La suspensión de epinefrina (Susphrine) no es un tratamiento adecuado en esta fase, pero se puede usar en los que mejoran como substitutiva de la segunda o tercera inyección de epinefrina.

La dosis de Susphrine es 0.005 ml/kg hasta un máximo de 0.15 ml. Debe ser la meta del tratamiento no continuar las inyecciones de susphrine cada 6 horas las 24 horas del día. De ser esto necesario debe pensarse que hay alguna falla en el tratamiento o alguna complicación que debe atenderse sin demora. Si las inyecciones de epinefrina no producen resultados favorables en 10 ó 20 minutos se puede administrar un agonista beta en aerosol. Por ejemplo, isoetarina (Bronkosol), metaproterenol (Metaprel o Alupent) o isoproterenol (Isuprel). Las dosis se presentan en la tabla 5. En algunos centros la aerosolterapia con los agonistas beta se ha empleado inicialmente en vez de epinefrina con buenos resultados.[5]

TABLA V

Dosis de los Agonistas Beta en Aerosol*	
Isoproterenol (Isuprel)	0.25 ml a 0.5 ml de la solución al 0.5%
Isoetarina (Bronkosol)	0.25 ml a 0.5 ml de la solución al 1%
Metraproterenol (Alupent)	0.1 a 0.3 ml de la solución al 5%

* Debe vigilarse la frecuencia cardíaca y si rebasa 200/min. Se interrumpe la aerosolterapia. Se administran las dosis recomendadas diluídas en 2 ml de solución salina normal empleando un nebulizador de mano o mecánico. (Maximist de Mead Johnson o De Vilbis 561). La frecuencia usual es cada 4 horas. Las dosis más bajas se emplean en los niños más pequeños. No se recomienda presión intermitente positiva IPPB ya que puede conducir a mayor resistencia de las aerovías, neumotórax y neumomediastino. El metaproterenol todavía no está aprobado oficialmente para uso en los niños menores de 12 años.

Xantinas. Las xantinas comprenden aminofilina, difilina y teofilina. La teofilina se usa por la vía oral y la aminofilina se recomienda únicamente por la vía endovenosa. La aminofilina oral no tiene ventajas sobre la teofilina y puede sensibilizar al enfermo a la etilenodiamina haciendo imposible la administración ulterior de aminofilina por la vía endovenosa.[6] A la vez que se comienza el tratamiento con epinefrina debe irse planeando la administración de aminofilina. Se averigua primero si el paciente ha tenido reacciones previas a la aminofilina y la cantidad de xantinas que ha recibido durante las últimas 24 horas; si es de larga o corta duración y cuándo fue la última dosis. Un paciente que hace más de 12 horas que no ha recibido la preparación regular de teofilina o aminofilina puede recibir las dosis usuales de aminofilina por la vía endovenosa. Si la preparación que ha recibido es de larga duración como por ejemplo, Slophyllin Gyrocaps, Somophyllin CRT, Theodur, Aerolate, Labid y otras parecidas, hay que tomar en consideración al calcular la dosis de aminofilina, las dosis de los preparados de larga duración recibidas durante las últimas 18 horas. Los pacientes que han recibido teofilina regular durante las últimas 12 horas o teofilina de larga duración durante las últimas 18 horas deben recibir la mitad de la dosis "normal" inicial de aminofilina; o sea, de 2 a 3 mg/kg. Otros factores que han de tomarse en consideración son los que aceleran la depuración de la teofilina y los que la demoran (Tabla 6). Estos son importantes, ya que pueden determinar la intoxicación por aminofilina o la falta de eficacia de la misma administrada en las dosis usuales.[7 8 9]. De ser posible, el tratamiento debe estar regido por las cifras sanguineas de teofilina. Estas deben medirse al comenzar el tratamiento, 1, 6 12 y 24 horas más tarde. Ulteriormente se miden con la frecuencia que sea necesaria dependiendo de la respuesta al tratamiento. La dosis de aminofilina se calcula preferiblemente a base del peso que el enfermo debiera tener de acuerdo con su estatura. La teofilina no se desplaza a los tejidos grasos; por esta razón, es que se calcula la dosis a base del peso "ideal". La dosis inicial es de 5 a 6 mg/kg y se administra durante un período de 20 a 30 minutos.[10] Luego se continúan dosis similares cada 6 horas o en infusión continua a base de 5 a 6 mg/kg cada 6 horas dependiendo de la edad. (Véase la tabla 7). En los infantes de 4 a 48 semanas de edad la dosis de teofilina por kg de peso debe ser menor que en los niños mayores. Se calcula como sigue:[11]

Dosis en mg/kg por *24 horas* = 8 + (0.3 x la edad en semanas)
Por ejemplo, la dosis de un infante de 27 semanas sería:
8 + (0.3 x 27) =
8 + 8.1 = 16 mg/kg/24 horas
Dosis cada 6 horas = 16/4 = 4 mg/kg cada 6 horas

En los niños mayores de 9 años y en los adultos la media vida de la teofilina es casi el doble de la de los niños de 1 a 9 años y se recomiendan dosis de mantenimiento más bajas que las de los niños de 1 a 9 años. Las dosis pueden aumentarse si se han medido las cifras séricas de teofilina y las mismas son insuficientes. La meta es alzanzar cifras de 12 a 18 microgramos por ml. Pero los incrementos deben hacerse con gran cautela (no más de 25%). Un incremento de 25% puede causar un aumento mayor de 50% en las cifras sanguíneas de teofilina. Por lo general, cada 0.5 mg/kg de teofilina produce un aumento de 1 microgramo por ml en la cifras séricas de teofilina.[10] Muchas veces no se conocen las cifras sanguíneas de teofilina y no hay datos precisos sobre la administración previa de teofilina. Si el paciente tiene dificultad respiratoria está justificado el riesgo de administrar una pequeña dosis de aminofilina por la vía endovenosa; se recomiendan 2.9 mg/kg de aminofilina (equivalente a 2.5 mg/kg de teofilina). Esta dosis se esperaría que produciría un aumento de 5 microgramos por ml en las cifras sanguíneas de teofilina. Las manifestaciones de toxicidad de aminofilina son nausea, vómitos, cefalea, hematemesis, excitación, convulsiones (cuando las cifras sanguíneas rebasan 40 microgramos por ml), taquicardia y arritmias. Sobredosis masivas de las xantinas han sido tratadas con hemoperfusión de carbón o resinas en los adultos y con exanguineotransfusión en los niños pequeños.[6]

La aminofilina por la vía endovenosa puede interrumpirse a las 24 horas o antes en los pacientes que mejoran. Pero se comienza la administración oral de teofilina alrededor de 3 horas antes de terminar el tratamiento por la vía endovenosa y se continúa el medicamento oral por 7 ó 10 días.

TABLA VI

Factores que Afectan la Depuración de la Teofilina o Aminofilina

Los siguientes aceleran la depuración y el paciente puede necesitar dosis más altas.

Fumar cigarrillos
Tratamiento prolongado con fenobarbital
Factores dietéticos (Exceso de proteínas)

Los siguientes demoran la depuración y las dosis deben reducirse.

	Reducción Recomendada
Fallo cardiaco	50% ó 0.2 mg/kg/hora
Hepatopatías	50% ó 0.2 mg/kg/hora
Insuficiencia respiratoria	30% ó 0.2 mg/kg/hora
Neumonía	No se ha establecido
Infecciones víricas febriles?	No se ha establecido
Eritromicina	(Efecto es inconsistente; sucede solo en alrededor de 1/3 de los casos)
Triacetiloleandomicina	No se ha establecido
Dejar de fumar cigarrillos	No se ha establecido
Tiabendazole	No se ha establecido
Cimetidine (Tagamet)	No se ha establecido
Propranolol (Inderal)	No se ha establecido
Vacuna de influenza	No se ha establecido
Obesidad	No se ha establecido
Exceso de carbohidratos	No se ha establecido

La Oxigenoterapia

Mientras se está administrando la aminofilina, si el paciente tiene dificultad respiratoria, debe administrársele oxígeno húmedo en concentraciones de 40%. El oxígeno no debe ser un tratamiento empleado como último recurso. Más bien debe administrarse temprano, por sonda nasal, para mantener la saturación de la Hb con oxígeno sobre 90%. Se recomiendan volúmenes de 4 a 5 litros de oxígeno por minuto (Tabla 8). En el niño asmático el oxígeno no causa la supresión de la respiración que se encuentra en el paciente con enfermedad crónica obstructiva del pulmón. El tratamiento con nebulizadores en tiendas de oxígeno no se recomienda por las siguien-

TABLA VII

Dosis de Aminofilina por la Vía Endovenosa en Pacientes que no han Estado Recibiendo Aminofilina o Teofilinas*

Edad	Dosis Inicial	Dosis durante las siguientes 12 horas	Dosis después de las 12 horas
11 meses a 9 años**	5 a 6 mg/kg	1.2 mg/kg/hora	1.0 mg/kg/hora
9 años a 16 años	5 a 6 mg/kg	1.0 mg/kg/hora	0.8 mg/kg/hora
Adultos no fumadores	5 a 6 mg/kg	0.7 mg/kg/hora	0.5 mg/kg
Pacientes mayores con cor pulmonale	5 a 6 mg/kg	0.6 mg/kg/hora	0.3 mg/kg/hora
Pacientes con fallo cardíaco congestivo o hepatopatías	5 a 6 mg/kg	0.5 mg/kg/hora	0.1-0.2 mg/kg/hora

* Las dosis indicadas son las de aminofilina. Para convertir éstas a teofinina multiplíquese por 0.83. Por ejemplo, una dosis de 24 mg de aminofilina = 20 mg de teofilina.
** Las dosis para infantes menores de 48 semanas de edad son más bajas que éstas. (Véase el texto para las recomendaciones específicas).

Fuentes: referencias 9 y 11.

tes razones: (a) las tiendas son reservorios de microorganismos patógenos, (b) la nebulización puede causar broncospasmo, (c) la temoregulación se obstaculiza, (d) la evaluación del enfermo se hace más difícil.[12] Una vez que la dificultad respiratoria haya cedido no debe prolongarse la oxigenoterapia innecesariamente ya que en dosis excesivas el oxígeno es un veneno tisular.

TABLA VIII

Concentraciones de Oxígeno Alcanzadas Mediante la Oxigenoterapia por Sonda Nasal

Volúmenes de oxígeno en litros por minuto	Concentración de oxígeno en %
1	24%
2	28%
3	32%
4	36%
5	40%
6	44%

Fuente: Shapiro, et al: Clinical Application of Blood Gases page 171, Year Book Medical Publishers, 1979.

Hidratación

La hidratación del asmático debe ser adecuada pero no exagerada ya que un volumen excesivo de líquidos puede conducir al edema pulmonar. Las soluciones administadas por lo general deben ser hipotónicas para suplir los requisitos aumentados de agua del niño asmático. Los volúmenes y contenido de los líquidos a ser administrados dependen de la valocación de las entradas y salidas de líquidos del paciente y variarían si hay vómitos, diarrea o fiebre. A continuación se ofrecen sugerencias sobre las dosis de líquidos endovenosos.[13] Pero las mismas deben ser consideradas como guías a variarse según la condición de cada enfermo.

A. Primera hora: glucosa al 5% en solución salina normal; 12 ml/kg ó 360 ml/metro cuadrado.

B. Mantenimiento: glucosa al 5% en agua; 50 a 60 ml/kg/24 horas ó 1500 ml/metro cuadrado/24 horas.

Con sodio: 30 mEq/litro y potasio (si la excreción urinaria es adecuada, 20 mEq/litro). Pueden emplearse las soluciones comerciales que contienen las concentraciones de electrolitos a éstas tales como Travert 4 e Ionosol WB.

C. Se añaden a éstos, si son necesarios, los volúmenes correspondientes a las pérdidas por vómitos, fiebre, etc. Hematocrito sobre 50% y peso específico de la orina sobre 1.025 señalan deshidratación. La meta debe ser bajar el peso específico urinario a cifras de 1.010.

Corticosteroides

Los corticosteroides están indicados en los pacientes que no mejoran durante las primeras 2 horas de tratamiento. Pueden emplearse hidrocortisona, metilprednisolona, betametasona y dexametasona. La dosis de hidrocortisona es 7 mg por kg por la vía endovenosa stat y 7 mg por kg durante las siguientes 24 horas en infusión continua. La dosis equivalente de metilprednisolona es de 1.7 mg/kg. La dexametasona y la betametasona se administran en dosis de 0.3 mg por kg stat y después la misma dosis (0.3 mg/kg) en infusión continua durante las siguientes 24 horas. La betametasona y la dexametasona son más eficaces que la hidrocortisona para aliviar la hipoxemia.[14] El efecto favorable se empieza a manifestar alrededor de las 3 horas pero no llega a su apogeo hasta alrededor de 24 horas. En este momento, si el paciente ha mejorado, se pueden administrar los corticosteroides por la vía oral por dos días más. Tratamientos cortos de 2 a 4 días se pueden interrumpir abruptamente. El tratamiento prolongado con corticosteroides debe evitarse. De ser necesario debe hacerse con prednisona preferiblemente en días alternos; *nunca* con beta-

metasona, dexametasona y otros corticosteroides análogos.

Los pacientes asmáticos que han recibido tratamiento prolongado con corticosteroides presentan un grave riesgo de insuficiencia de la suprarrenal durante un ataque agudo de asma u otra situación de "stress" agudo. El riesgo persiste alrededor de 1 a 2 años después de haberse interrumpido los corticosteroides. En estos casos el tratamiento con corticosteroides debe comenzarse inmediatamente, continuarse hasta que la situación de "stress" haya pasado y luego interrumpirse gradualmente. Idealmente, deben medirse las cifras sanguíneas de cortisol antes de interrumpir el tratamiento con corticosteroides totalmente.

vida. Se recomienda una dosis de 1.5 mEq/kg en una infusión lenta que no rebase 10 mEq por minuto.[15] Cuando se conocen las cifras de déficit de base la dosis se puede calcular como sigue: Dosis de bicarbonato = 0.3 x peso en kg x déficit de base en mEq.[16]

Atropina en Aerosol

La atropina se puede ensayar en los pacientes que no mejoran con la teofilina, los beta adrenérgicos y los otros tratamientos. La dosis es de 0.05 mg/kg cada 6 horas. Es

TABLA IX

Ejemplo de la Evaluación de un Caso Hipotético de un Niños Asmático por Medio de los Datos de la Exploración Clínica

Estado Asmático	Frecuencia Cardíaca	Pico del Flujo Espiratorio/% de lo esperado	Puntuación Clínica (Fig. 1)	Pulso Paradójico	Horas de Tratamiento
Grave	180	5%	7	40	0
Empezando a mejorar	140	10%	5	30	6
Continía mejorando	130	15%	3	20	12
Continúa mejorando	125	25%	2	10	18
Continúa mejorando	120	25%	1	5	24
Considerable mejoría	112	58%	1	0	30

Trastornos del Equilibrio Acido Base y Oxigenación

El desequilibrio de la ventilación-perfusión es el causante principal de la hipoxemia. Esta conduce a la hiperventilación. Más tarde la obstrucción progresiva determina hipoventilación y retención de CO_2. La interpretación correcta de los resultados de la medición de los gases arteriales es de gran importancia. La correlación entre éstos y las distintas etapas del asma bronquial se presenta en la fig. 3. A principio las cifras de CO_2 y O_2 disminuyen gradualmente ya las de pH se mantienen estables. A medida que progresa el ataque y hay hiperventilación las disminuciones de CO_2 y O_2 se acentúan y las de pH aumentan. Cuando no hay mejoría las cifras de CO_2 aumentan y las de pH y O_2 disminuyen. Esto asegura la insuficiencia respiratoria. El tratamiento con bicarbonato puede estar indicado cuando las cifras de pH arteriales son menores de 7.3 y las del déficit de base mayores de 5 mEq/litro. El bicarbonato es un medicamento para usarse cuando la acidosis pone en peligro la vida del enfermo. Es una medida temporal empleada para evitar acidosis incompatible con la

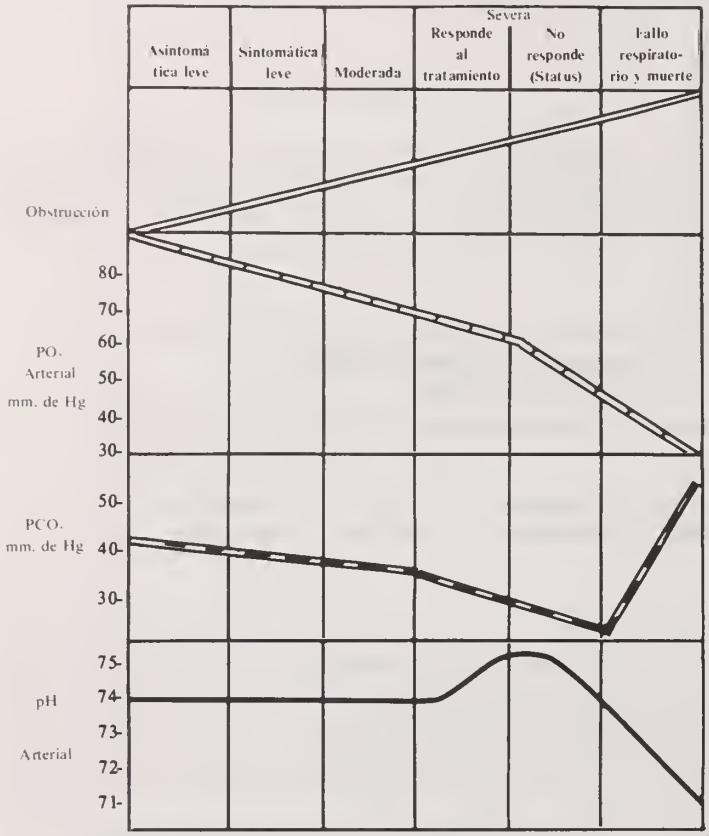
preferible empezar con las dosis más bajas ya que el fármaco se absorbe en la circulación general y puede causar toxicidad. El medicamento se absorbe en las mucosas respiratorias rápidamente y aparece en el suero durante los primeros 15 minutos persistiendo hasta 4 horas. La absorción puede ser lo suficientemente alta para causar síntomas tales como visión nublada, debilidad, boca seca y taquicardia.[17]

Difilina

La difilina es una xantina cuyo uso rutinario no se recomienda. Podría ser útil cuando existe dificultad para administrar la aminofilina por la vía endovenosa o cuando hay problemas de alergia a la aminofilina. La dosis de difilina no está bien establecida. Se ha recomendado administrar 4 mg/kg por la vía intramuscular.[6] La media vida del medicamento es de 2 horas. Por peso molecular el 70% de la difilina consiste en teofilina pero ésta no se convierte en teofilina libre y el 85% de la difilina se excreta en la orina como tal. Las cifras

FIGURA III

Etapas del Asma Bronquial



De: Sifontes, J.E., Mayol, P.M., Rodríguez-Martínez, F. y Valcárcel, M. Neumología Pediátrica, Universidad de Puerto Rico, Reciento Universitario de Ciencias Médicas, 1974. pág. 123. Gráfica adaptada y modificada de Chai y Newcomb, Am J Dis Child. 125:757, 1973.

séricas de difilina deben medirse separadamente de las de teofilina. Las cifras séricas de teofilina en los pacientes que reciben difilina no pueden emplearse como guías para hacer ajustes en las dosis de ninguno de los dos medicamentos.[18]

La Insuficiencia Respiratoria

Los criterios para el diagnóstico de insuficiencia respiratoria son: (a) retracciones en la inspiración, (b) disminución de los ruidos respiratorios inspiratorios, (c) hiperinflación con diminución de los movimientos respiratorios, (d) obnubilación con respuesta disminuida al dolor, (e) cianosis o cifras de paO_2 menores de 70 mm Hg en oxígeno al 40%, (f) PCO_2 sobre 60 mm Hg o aumentos de PCO_2 de más de 5 mm Hg por hora, [12] o (g) cifras de PaO_2 menores de 50 mm Hg en O_2 al 100% o de PCO_2 mayores de 50 mm Hg.[16]

Los criterios f y g se aplican a los pacientes agudamente enfermos y no a los que sufren de enfermedad crónica pulmonar que pueden tener trastornos previos de las cifras de CO_2 y O_2.

La insuficiencia respiratoria debe tratarse mediante la ventilación mecánica aunque recientemente algunos expertos han recomendado la terapéutica con isoproterenol por la vía endovenosa para evitar la ventilación mecánica.

Tratamiento con Isoproterenol. El tratamiento con isoproterenol por la vía endovenosa conlleva riesgos que hacen necesaria la administración con gran cautela, en la unidad de cuidado intensivo, con la atención continua de un facultativo experto en esta forma de tratamiento. Se emplea una solución de 1 mg de isoproterenol en 100 ml de glucosa al 5% de agua. La concentración de isoproterenol así diluido es de 10 microgramos por ml ó 0.1 microgramos por 100 ml.[12]

Se administra en ciclos de 2 horas en las siguientes dosis:

Tiempo del ciclo en minutos	Microgramos x kg/minuto	ml/kg/minuto
0	0.1	.01
20	0.2	.02
40	0.3	.03
60	0.4	.04
80	0.5	.05
100	0.6	.06
120	0.7	.07

Se empieza con 0.1 microgramos por kg por minuto. Se aumenta la dosis cada 20 minutos en incrementos de 0.1 microgramos por kg. La mejoría puede suceder en 20 minutos o puede tardar 4 horas ó más. Hasta tanto haya una mejoría se repiten los ciclos de 120 minutos administrando las dosis señaladas en la tabla cada 20 minutos después de los 120 minutos previos. O sea, se vuelve a empezar con 0.1 microgramos por kg y se aumenta la dosis a razón de 0.1 microgramos por kg cada 20 minutos.

Los volúmenes señalados se administran por infusión continua a la vez que se miden cada 20 minutos la presión arterial y las cifras arteriales de gases y pH. La infusión se interrumpe cuando las cifras de CO^2 bajan de 50 mmHg, si la frecuencia cardíaca rebasa 200/minuto o si aparecen arritmias. Cuando la respuesta es favorable la frecuencia cardíaca aumenta a 170 ó 180, se estabiliza en estas cifras o disminuye. Esto suele suceder al llegar a las dosis entre 0.4 y 0.7 micorgramos/kg por minuto de isoproterenol. La dosis que produce mejoría se continúa por 12 horas y después se disminuye a razón de 0.1 microgramos/kg por minuto (o menos) por hora, guiándose por la medición de los gases y pH arteriales. Se descontinúa el tratamiento a las 36 horas después de comenzado a menos que aparezca el broncopasmo nuevamente. La complicación principal es arritmia que puede conducir a isquemia cardíaca y muerte.

La Ventilación Mecánica.

El tratamiento por medio de la ventilación mecánica está indicado cuando las cifras de PCO_2 van en aumento y se mantienen sobre 55 mm HG. Se prefiere la intubación nasotraqueal. Durante la intubación debe administrarse oxígeno al 100% y las secreciones deben aspirarse según sea necesario. El contenido gástrico debe aspirarse contínuamente por sonda nasogástrica. Para realizar la ventilación mecánica se requiere el bloqueo neuromuscular. Se administran diezapam (Valium), 0.1-0.3 mg/kg ó pancuronium (Pavulon) 0.05 a 0.08 mg/kg.

Este es preferible al d-tubocurarine ya que pancuronium no afecta el sistema cardiovascular ni produce liberación de histamina. Se prefiere la ventilación controlada por volumen la cual provee las presiones necesarias para la ventilación adecuada independientemente de la resistencia y permite el control más preciso de la oxigenación.[12] Las complicaciones de la ventilación mecánica, además de las posibles fallas del equipo o la electricidad, comprenden oxigenotoxicidad, infecciones secundarias, atelectasia, neumotórax, neumomediastino y las relacionadas con la intubación. La sonda traqueal puede obstruirse, puede ser expulsada o puede estar mal ubicada y obstruir un bronquio principal. Hemorragias nasales, úlceras, granulomas y estenosis subglótica pueden suceder. A pesar de estas complicaciones muchos expertos todavía prefieren la ventilación mecánica al isoproterenol por la vía endovenosa.

Fisioterapia Pulmonar

La fisoterapia pulmonar y la succión de las secreciones de estos enfermos pueden ser de vital importancia para su recuperación, pero a su debido tiempo. Un paciente cianótico con dificultad respiratoria aguda no debe someterse a una sesión de fisioterapia pulmonar. Si se sospechan secreciones espesas como la causa de la cianosis puede ser este el momento apropiado par asuccionar la orofaringe y la traquea. La succión debe hacerse en forma que no se traumaticen las mucosas. Una sonda muy rígida introducida repetidas veces bruscamente puede traumatizar la mucosa y causar edema o hemorragia de la misma. Cuando el paciente se estabiliza los cambios de posición y los palmoteos suaves pueden comenzarse para facilitar el drenaje de las secreciones. En los pacientes tratados con ventilación mecánica la fisioterapia pulmonar es parte fundamental de la atención integral de los mismos.

Otros tratamientos —Los antitusivos y sedantes están contraindicados en estos pacientes. Los antihistamínicos no tienen efectos sobre el grado de broncoconstricción exceptuando promethazine (Phenergan) que puede causarla y chlorfeniramina que en dosis altas puede ejercer un efecto broncodilatador.[2] Los antimicrobianos están indicados si hay evidencia de infección bacteriana pero no como medida profiláctica. Los llamados expectorantes y el yodo no benefician estos pacientes y pueden causar reacciones adversas tales como erupciones o vómitos. La administración de aspirina debe evitarse en los niños asmáticos ya que se encuentra intolerancia en alrededor del 28% de los que son atópicos.[6]

Seguimiento — Cuando se dá de alta al enfermo es el momento de comenzar nuevamente el tratamiento preventivo. Debe verse dos o tres días más tarde en la consulta externa. Mientras tanto, debe continuársele el tratamiento con broncodilatadores y, además, corticosteroides o antimocrobianos si éstos han sido utilizados como parte del tratamiento de urgencia. Si el paciente empeora antes de la cita debe sentirse en libertad de llamar a su médico o regresar prontamente a la sala de emergencias. Los corticosteroides generalmente pueden interrumpirse a los 2 ó 3 días. Los broncodilatadores deben continuarse por 7 ó 10 días ya que, a pesar de que no haya signos físicos positivos, los trastornos obstructivos persisten por varios días.

En los pacientes refractarios a tratamiento que necesitan hospitalizaciones repetidas los factores sicosomáticos pueden jugar un papel importante. Para la atención de estos casos se ha sugerido la creación de unidades especiales para estadía prolongada en el hospital y tratamiento sicosomático en colaboración con todo el equipo de los servicios de la salud y los siquiatras de niños.[19]

Summary **The asthmatic patient who arrives at the emergency room should be evaluated and managed immediately. The following outline of management is suggested: (1) History and physical examination rapidly performed and directed to what is relevant. (2) Identify promptly the patients who may be managed in the emergency room or who need hospitalization. (3) Treat with epinephrine and, if available, with beta 2 agonists in aerosol. (4) if there is no significant prompt improvement, administer aminophylline by the intravenous route. (5) Oxygen therapy. (6) Adequate but not excessive hydration. (7) Corticosteroids without delay —do not wait for the patient to deteriorate. (8) Record progress in flow graphs or tables in which the following are noted at 1/2, 1, 2 or 3 hour intervals as needed (table 9): (a) clinical score, (b) peak flow rates or spirometry (if available), (c) bood pressure, cardiac and respiratory rates, (d) blood theophylline levels (if done), (e) arterial bood gases (if done). (9) Laboratory tests as indicated: (a) chest roentgenograms, (b) complete blood count including hematocrit, (c) urinalysis including specific gravity, (d) stools for ova and parasites, (e) tuberculin test, (f) blood gases and electrolytes. (10) If hospitalization is needed his should be at the intensive or special care unit where the patient can be monitored continually until stabilized.**

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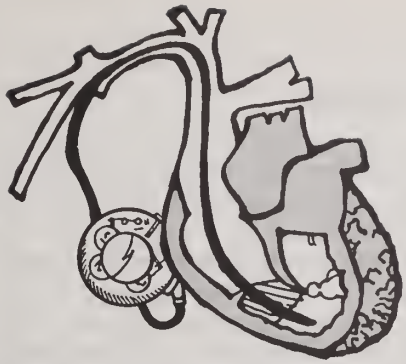
"Desde la cúspide de la Torre de la Luz pude captar mis impresiones más fascinantes de San Juan. La vista panorámica desde este punto es singularmente bella. Las salas interiores abiertas, llamadas "patios", de las residencias privadas, cada una con un fresco y floreciente criadero de árboles y plantas; los parapetos cubiertos de musgo que los separan de la vista más abajo. Las calles estrechas, serpentinas, a sus costados las casas compactamente unidas, con paredes raramente embellecidas en tonos naturales".

"Hacia un lado un delicioso jardín público adornado con plantas ornamentales nativas entre las que reconocí la Higuera; el Tamarindo, y el Alhelí. En su centro hay un espléndido monumento a Cristobal Colón".

Descripción de Don José de Olivares, "reconocido autor y corresponsal de guerra". 1899.



Indicaciones para Uso de Marcapasos Permanentes; Tendencia Actual

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Resumen: **El propósito de este estudio es evaluar nuestra experiencia e indicaciones durante los pasados 10 años en la implantación de marcapasos permanentes en el Hospital de Veteranos. Con este propósito se revisaron retrospectivamente los expedientes clínicos de todos los pacientes con marcapasos permanentes seguidos en la clínica de marcapasos. En 77 de estos pacientes se documentó objetivamente la indicación inicial y se pudo evaluar el seguimiento médico después de la implantación de marcapasos permanente. Encontramos que la incidencia de bloqueo bifascicular y síndrome de nodo sinusal enfermo sintomático ha aumentado como indicación para implantación de marcapasos permanente en la población de veteranos.**

La menor morbilidad perioperatoria en la implantación del marcapasos permanente, mayor longevidad del generador del pulso y un mejor seguimiento postoperatorio, han expandido y aumentado las indicaciones clínicas para la implantación de los marcapasos permanentes.

Las indicaciones para uso de marcapasos permanentes (MP) han cambiado gradualmente en los últimos años. La baja morbilidad en su implantación, mayor longevidad y mayor grado de perfeccionamiento técnico del generador de pulso son los factores que han motivado estos cambios.[1 2] Las indicaciones más frecuentes son las siguientes:[3 4 5 6] bloqueos bifascinantes sintomáticos, bloqueos atrio ventriculares sintomáticos de segundo y tercer grado, enfermedad del nodo sinusal sintomática, taquiarritmias supraventriculares y ventriculares refractarias a tratamiento médico y estados de bajo gasto cardíaco o bradicardia o disociación atrio ventricular.

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El propósito de este estudio es el de evaluar nuestra experiencia e indicaciones durante los pasados dies años en la implantación de marcapasos permanentes en el Hosptial de Veteranos de San Juan, Puerto Rico.

Materiales y Métodos

Se revisaron retrospectivamente los expedientes clínicos de todos los pacientes con marcapasos permanentes (MP) implantados en el Hospital de Veteranos durante los años 1969 al 1979. De igual forma se estudiaron los expedientes médicos de todos aquellos pacientes con MP referidos de otras instituciones para seguimiento en nuestro hospital.

Durante este período de tiempo se evaluaron 105 pacientes con MP seguidos en la clínica de marcapasos del Hospital de Veteranos. En 77 de estos pacientes se documentó objetivamente la indicación inicial y se pudo evaluar el seguimiento médico después de la implantación de MP.

Los 77 pacientes fueron divididos en dos grupos: el grupo I consistió de 26 pacientes con MP implantados entre los años 1969 al 1974. El grupo II consistió de 51 pacientes con MP implantados entre 1975 al 1979.

En ambos se evaluó la edad promedio del paciente, indicación para el implante de MP, complicaciones a corto y largo plazo, al igual que el método utilizado para la implantación. Se utilizó la prueba exacta de Fisher para el análisis estadístico. Valores de p menor de .05 fueron considerados estadísticamente significativos.

Resultados

Las edades de los pacientes del grupo I fluctuaron entre 73 a 91 años con un promedio de 73 años. Las del grupo II fluctuaron entre 48 a 92 años con un promedio de 71 años. No hubo diferencias estadísticas en ambos grupos.

La Tabla I ilustra las indicaciones para uso de MP en los pacientes estudiados. Las indicaciones más frecuentes fueron bloqueo atrio-ventricular completo, bloqueo bifascicular, fibrilación atrial con respuesta ventricular lenta, síndrome del nodo sinusal enfermo e hipersensitividad carotídea.

El bloqueo atrio-ventricular completo fue la indicación más frecuente en el grupo I (84%). Sin embargo, aunque también lo fue en el grupo II (51%), la diferencia es estadísticamente significativa. ($p<0.001$). En el grupo II la segunda indicación más frecuente fue el bloqueo bifascicular sintomático (21%), mientras que solamente un paciente del grupo I recibió MP por esta condición ($p<0.05$).

Las complicaciones más frecuentes encontradas en ambos grupos ha sido tabulada en la Tabla II. Fallo de batería e infección en el lugar de implantación del generador de pulso fueron las complicaciones más frecuentes en el Grupo I. En dos pacientes del Grupo II, el generador de pulso tuvo que ser reemplazado por defectos intrínsecos de la misma ($p<0.001$). Todos los pacientes del Grupo I recibieron generadores de pulso con baterías de mercurio, mientras que los del Grupo II recibieron generadores de pulso con baterías de litio.

La incidencia de infecciones en el lugar de implante disminuyó significativamente de 38% el Grupo I a 14% en el Grupo II ($P<.05$).

TABLA I

Indicaciones para uso de MP en 77 pacientes estudiados en el Hospital de Veteranos

Indicaciones	GRUPO I No.	%	GRUPO II No.	%	Valor de P
Bloqueo A V Completo	22	84	26	51	<0.05
Bloqueo bifascicular	1	4	11	21	<0.05
Fibilación atrial con respuesta ventricular lenta	1	4	1	2	NS
Síndrome del nodo sinusal enfermo	2	8	11	21	NS
Hipersensitividad carotidea	—	—	2	5	NS
TOTAL	26	100	51	100	

TABLA II

Complicaciones de los 77 pacientes estudiados en el Hospital de Veteranos

Complicaciones	GRUPO I No.	%	GRUPO II No.	%	Valor de P
Fallo de Batería	26	100	2	4	<0.001
Infecciones	10	38	7	14	< 0.05
Fractura del Electrodo	2	8	—	—	NS
Migración del Electrodo	—	—	3	6	NS

TABLA III

Relación de los dos tipos de implantes de MP en los 77 pacientes estudiados en el Hospital de Veteranos

	GRUPO I		GRUPO II	
Complicación	Endocárdico (8)	Epicárdico (18)	Endocárdico (43)	Epicárdico (8)
Infecciones	5	5	7	—
Fractura Catéter	—	2	—	—
Migración Catéter	—	—	3	—

La Tabla III demuestra el lugar de implantación del electrodo en ambos grupos de pacientes. La mayoría de los catéteres fueron colocados en la pared epicárdica del ventrículo derecho o izquierdo en el Grupo I (18/26). Sin embargo, solo el 16% del Grupo II (8/51) recibieron catéteres epicárdicos; la mayoría fueron endocárdicos colocados en el ápice del ventrículo derecho. Como se puede ver en la Tabla III, la incidencia de infecciones fue relativamente menor en el Grupo II, (7/51) que en el Grupo I (10/26). Sin embargo al compararse la incidencia de infecciones en los MP epicárdicos de ambos grupos (5/26), ésta no es estadísticamente significativa ($p > .05$) a la incidencia de infecciones (12/51) en los endocárdicos. La incidencia de fractura de catéter aunque relativamente baja en el Grupo I, solamente la hemos observado en los catéteres epicárdicos. En nuestra serie, la migración del catéter parece ser más frecuente en los catéteres de implantación endocárdica.

Discusión

El bloqueo atrio-ventricular completo siguie siendo la indicación principal para implantación de MP en el Hospital de Veteranos. El bloqueo bifascicular le sigue en importancia, probablemente debido a que se están refiriendo para estudio electrofiológico un mayor número de pacientes con bloqueo bifascicular sintomático y bloqueo atrio-ventricular completo intermitente y transitorio.

El síndrome del nodo sinusal enfermo sintomático como indicación para MP, ha ido aumentando en la población de veteranos, posiblemente debido a un mayor entendimiento de su patofisiología y manifestaciones clínicas. La fibrilación atrial con respuesta ventricular lenta y el síndrome de hipersensitividad carotídea son indicaciones poco frecuentes en nuestra serie.

El fallo de batería en el Grupo I mayor que en el Grupo II, se debió a que en los primeros pacientes se emplearon baterías

de mercurio, cuya longevidad era de uno a dos años. Los del Grupo II utilizaron baterias de litio,[14 15 16] cuya duración es de diez a quince años. El Grupo I tuvo un seguimiento mayor, lo cual contribuyó a este mayor fallo de baterías.

El perfeccionamiento de las técnicas de implantación de MP, major cuidado perioperatorio y el seguimiento efectivo de los pacientes con MP, fueron algunos de los factores responsables por la disminución,[7 20] de infecciones en el Grupo II.

Se prefiere en el Hospital de Veteranos implantar MP endovenosos en pacientes mayores de edad con problemas de fibrosis cardíaca (infarto, cardiomiopatías), ya que al implantarse en el endocardio del ventrículo derecho, menos afectado por estos procesos patológicos, hay mejor mecanismo de captura con una baja resistencia a la estimulación cardíaca por el MP. En pacientes jóvenes con el síndrome del nodo sinusal enfermo, preferimos la implantación epicárdica en el ventrículo izquierdo, ya que aquí se logran mejores parámetros de captura y senseo. Además la duración de los electrodos epicárdicos ha sido bien documentada por largos años.

La fractura del electrodo ocurre mayormente en los electrodos epicárdicos, pero es rara esta complicación. La migración del electrodo ocurre mayormente en los electrodos endocárdicos y ocurre en aquellos casos en que hay dilatación del ventrículo derecho. Esta complicación ha disminuído con el uso de los electrodos "tinned", los cuales ofrecen una mayor superficie lateral en el electrodo para que se encaje en las trabéculas del ventrículo derecho y se fije por fibrosis secundaria.

En conclusión, tenemos en los bloqueos bifasciculares y síndrome del nodo sinusal enfermo sintomáticos han aumentado como indicación para implantación de MP en la población de veteranos. La menor morbilidad perioperatoria en la implantación del MP, mayor longevidad del generador del pulso y un mejor seguimiento post-operatorio han expandido y aumentado las indicaciones clínicas para la implantación de MP.

Summary: The ten year experience of permanent pacemaker placement at the Veterans Administration Hospital was assessed. A retrospective review of the medical records of all the patients with permanent pacemakers was performed. In 77 of such patients the indication for insertion was documented objectively and the post-pacemaker follow up could be properly evaluated. There was an increase in the incidence of bifascicular block and sick sinus syndrome as indication for permanent pacemaker insertion in our population.

The low perioperative morbidity in permanent pacemaker implantation together with the longer survival of the pulse generator and a better post operative follow up has expanded the clinical indications for permanent pacemaker insertion.

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"I'll give it to you straight . . . You have a Super-Hernia . . ."

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Esquistosomiasis: Espectro Clínico de la Enfermedad y Respuesta a Tratamiento con Oxamniquina en Infecciones Crónicas

Resumen: La esquistosomiasis en un problema de salud muy común en Puerto Rico donde se ha reportado una prevalencia de hasta 35% en algunas comunidades.

En este estudio comprobamos la eficiencia de la nueva droga oxamniquina en curar personas con la enfermedad crónica con o sin síntomas y/o signos de la enfermedad.

La esquistosomiasis continua siendo un problema alarmante de salud pública en Puerto Rico y otros países tropicales. La endemicidad de esta parasitosis ha sido comprobada anteriormente en nuestra Isla, habiéndose encontrado una prevalencia de hasta 35% en comunidades estudiadas.[1]

Los esfuerzos terapeúticos contra esta enfermedad no fueron verdaderamente efectivos hasta el descubrimiento de oxamniquina. Esta droga ha demostrado su eficacia en infecciones crónicas en pacientes adultos puertorriqueños excretando 100 o más huevos por gramo,[2] así como en pacientes pediátricos con esquistosomiasis aguda con todas las intensidades de infección.[3]

El objetivo de este estudio fue evaluar la eficacia y seguridad de oxamniquina oral en pacientes de todas las edades con esquistosomiasis crónica, con particular énfasis en infecciones de 50 o menos huevos por gramo. El espectro clínico de la enfermedad en nuestro grupo de pacientes también fue evaluado.

Materiales y Métodos

Nuestra población consistió de 47 pacientes de ambos sexos, de 10 hasta 63 años de edad, con evidencia clínica y/o laboratorio de esquistosomiasis crónica. A todos los pacientes se les efectuó un historial médico con particular énfasis en la sintomatología característica de esquistosomiasis crónica, así como un examen físico completo. Todos los sujetos fueron sometidos a las siguientes pruebas: hemograma, urinálisis, conteo de eosinófilos, función hepática y examen coprológico usando el método de concentración Ritchie modificado.[4] Algunos pacientes ya estaban diagnosticados con métodos directos de corpología al llegar a nuestras clínicas. Otros pacientes fueron sospechados por la prueba circumoval positiva y confirmados luego. A los pacientes que clínicamente presentaron evidencia de envolvimiento hepatoesplénico se les efectuó un escintigrama de hígado y bazo. Los sujetos que a pesar de presentar clínica de esquistosomiasis crónica tuvieron coprologías negativas por el método Ritchie se les practicó una biopsia retal con fines diagnósticos. Dos pacientes habían sido previamente diagnósticados de esquistosomiasis crónica hepatoesplénica por biopsia hepática.

Se dividió la población por grupos etáreos. También se clasificaron en cuatro grandes categorías clínicas a saber:

Esquistosomiasis Intestinal Asintomática:

Pacientes que en evaluación rutinaria presentaron huevos viables de Schistosoma mansoni en heces, pero que no tenían sintomatología intestinal asociada ni evidencia de envolvimiento hepatoesplénico.

Esquistosomiasis Intestinal Sintomática:

Pacientes donde había evidencia de síntomas gastrointestinales como molestias y dolores abdominales recurrentes, diarrea, anorexia, dispepsia, hematoquezia, pero que no tenían envolvimiento hepatoesplénico.

Esquistosomiasis Hepatoesplénica Asintomática:

Estos pacientes estaban excretando huevos de S. mansoni, eran completamente asintomáticos y en el examen físico se les encontró evidencia de hepato y/o esplenomegalia no atribuible a otras causas. Se les practicó un scintigrama de hígado y bazo que fue confirmatorio.

Esquistosomiasis Hepatoesplénica Sintomática:

Sujetos con enfermedad avanzada, hepatoesplenomegalia, hipertensión portal, ascites, con debilidad, dolor y distensión abdominal, diarreas con sangre y otros síntomas asociados.

Después de educar a los pacientes sobre el uso de oxamniquina, se les administró esta droga por vía oral en dosis de 15 mg/kg adultos y 20 mg/kg niños. Se siguieron estos

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pacientes mensualmente y se repitieron las pruebas de laboratorio pertinentes durante el año subsiguiente.

En 23 pacientes se determinó la intensidad de infección por el método Ritchie modificado dividiéndolos en grupos de excreción de 1-50 HPG, 51-100 HPG y mayor de 100 HPG. Se definió cura cropológica como la ausencia de huevos de S. mansoni en heces fecales, tres meses después de tratamiento.

Resultados

La Tabla 1 nos ilustra la frecuencia de los diferentes métodos de diagnóstico en nuestra población. El método de concentración Ritchie modificado fue el más frecuentemente utilizado (65). Algunos de nuestros pacientes fueron diagnósticados por dos o más de estos métodos.

TABLA I

Métodos Diagnósticos Utilizados en 47 Pacientes con S. Mansoni

	Ritchie Mod.	Coprología Directa	Biopsia Rectal	Biopsia Hepática
Frecuencia de Método Diagnóstico	33	12	5	2
%	65%	23%	10%	4%

El espectro clínico de la enfermedad en nuestra población está ilustrado en la Tabla II. Veintiún pacientes (45%) presentaron esquistosomiasis intestinal asintomática, 18 pacientes (38%) intestinal sintomática, 4 sujetos hepatoesplénica sintomática y 4 pacientes hepatoesplénica asintomática.

TABLA II

Espectro Clínico en 47 Pacientes con Esquistosomiasis Crónica

Clasificación	No. Pacientes	% Pacientes
Intestinal Asintomática	21	44.7
Intestinal Sintomática	18	38.3
Hepatoesplénica Asintomática	4	8.5
Hepatoesplénica Sintomática	4	8.5
Total	47	100%

La oxamniquina fue altamente efectiva en obtener una cura coprológica en diferentes niveles de intensidad de infección. Tanto en el grupo excretando de 1-50 HPG como en el de 51-100 HPG se obtuvo un 100% de cura a los tres meses después de tratamiento. En el grupo excretando 100 ó más huevos por gramo el porciento de cura fue de 85. Estos hallazgos son estadísticamente significativos. (Tabla III)

La tabla IV nos ilustra el porciento de cura en los diferentes grupos de edades estudiados. Se obtuvo un 100% de cura en todos los grupos excepto en el de 41-50 años donde se trataron dos pacientes y uno de éstos, que inicialmente estaba excretando 242 HPG, presentó una excreta positiva de 1 HPG a los tres meses post tratamiento. Aunque no tuvo una completa cura coprológica, la reducción fue significativa. El porcentaje de cura total fue de 96%. Esto es estadísticamente significativo.

TABLA III

Efectividad de Oxamniquina en Diferentes Intensidades en Infección por S. Mansoni

Intensidad de Infección (Huevos/Gramo Heces)*	No. Pacientes Tratados	No. Pacientes Curados**	% Cura
1-50	11	11	100
51-100	5	5	100
Más de 100	7	6	85

* Método Diagnóstico Ritchie Modificado.
** Tres meses Post-tratamiento.

Los efectos secundarios de la droga fueron en su mayoría transitorios y bien tolerados por los pacientes. No hubo diferencia significativa de los reportados anteriormente en la literatura mundial y en Puerto Rico. Predominaron el cambio en coloración de la orina, vértigo, somnolencia y molestias abdominales.

TABLA IV

Efectividad de Oxamniquina en Pacientes con Esquistosomiasis Crónica por Grupos de Edades

	Núm. pacientes tratados	Núm. pacientes curados (Ritchie Mod. negativo)	Porciento de cura
0 - 10 años	1	1	100%
11 - 20 años	11	11	100%
21 - 30 años	2	2	100%
31 - 40 años	6	6	100%
41 - 50 años	2	1	50%
51 ó más	1	1	100%
Total	23	22	95.6%

Discusión

Hemos observado como en nuestra serie de 47 pacientes con esquistosomiasis crónica existe una amplia variedad de manifestaciones clínicas que van desde la forma intestinal asintomática hasta el envolvimiento visceral hepatoesplénico con sintomatología severa. Más de 50% de los pacientes no presentaban síntomas específicos y fueron diagnósticados por evaluaciones rutinarias de sus médicos primarios. Es importante notar que ocho pacientes tenían envolvimiento hepatoesplénico en el momento del diagnóstico y que la mitad de estos estaban asintomáticos. Estos hallazgos demuestran que la sintomatología no es necesariamente buen indicador para sospechar infección por bilharzia en todos los casos y que la enfermedad puede progresar, sin síntomas hasta el envolvimiento visceral. Esto apoya la aseveración del doctor Marcial en estudios de Sotomayor y colegas de que en nuestra isla existen muchos pacientes completamente asintomáticos con infección de S. mansoni aún sin diagnósticar.[5 6] Esto también refuerza la idea de que la comunidad médica necesita más accesibilidad a métodos sensitivos de diagnóstico como el Ritchie modificado, y que definitivamente necesitamos estudios de comunidades en áreas sospechadas como endémicas para verdaderamente evaluar la magnitud del problema en Puerto Rico.[7 8 9]

La efectividad de oxamniquina en pacientes excretando 50 o menos huevos por gramo no había sido estudiada anteriormente en Puerto Rico. En nuestra serie se obtuvo un 100% de cura en once pacientes de esta categoría así como en los pacientes excretando 51-100 HPG. La droga fue bien tolerada y los efectos secundarios fueron transitorios. Aunque nuestra población fue pequeña, estos hallazgos nos indican que todo paciente con esquistosomiasis crónica, particularmente el que está excretando 50 ó menos huevos por gramo, debe ser tratado con oxamniquina si no hay contraindicación médica a su uso. Esto disminuiría el riesgo de envolvimiento visceral a largo plazo y la propagación de la parasitosis. Obtuvimos una respuesta de cura de 95% en todos los grupos de edades y por lo tanto podemos afirmar que esta droga es altamente eficaz en todas las generaciones de puertorriqueños padeciendo de esta enfermedad.

Podemos entonces concluir que:

1. La data indica que la mayoría de nuestros pacientes presentaron esquistosomiasis crónica en su forma intestinal asintomática, aunque hubo un porciento significativo de envolvimiento hepatoesplénico.
2. La oxamniquina, en una dosis de 15-20 mg/kg de peso corporal fue altamente efectiva en todos los grupos de edades y todas las intensidades de infección especialmente en infección de menos de 50 huevos por gramo.
3. Recomendamos tratamiento con oxamniquina a todos los pacientes con esquistosomiasis crónica particularmente a los que están excretando menos de 50 huevos por gramo, si no hay otras contraindicaciones médicas. Detectando tempranamente esos pacientes estaremos haciendo una medicina preventiva eficaz y contribuiremos al control de esta parasitosis en nuestra Isla.

Summary: **Schistosomiasis is a very common health problem in Puerto Rico where some communities have a reported prevalence of 35%.**

We proved the effectiveness of the new drug oxamniquine in curing persons with chronic schistosomiasis with or without signs and symptoms of the disease.

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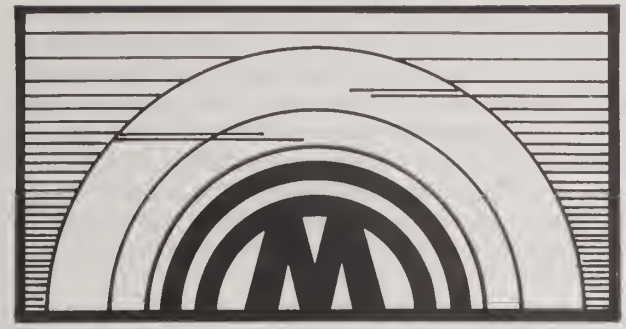

MEDICINA AL DIA

José A. Alvarez-Ruiz, MD

Reflujo Gastroesofágico en Pediatría

Resumen: El reflujo gastroesofágico es un problema pediátrico común asociado a una morbilidad considerable. Las complicaciones más frecuentes y severas son enfermedades pulmonares recurrentes y detención del crecimiento. Varias modalidades diagnósticas son utilizadas para su detección temprana siendo el estudio de pH esofágico la más sensitiva. Las medidas mecánicas y físicas son la base del manejo, reservándose la cirugía para aquellos casos con complicaciones severas.

El reflujo gastroesofágico (GE) con o sin hernia de hiato ocurre a cualquier edad. El espectro de síntomas es diferente en infantes y adultos. En los infantes puede manifestarse por vómitos, retraso en el crecimiento neumonía por aspiración, esofagitis y episodios apneicos.

Observaciones clínicas han confirmado que la visualización radiológica o endoscópica de herniación gástrica a nivel del hiato no es un requisito para el diagnóstico de reflujo GE patológico en los infantes. La única anormalidad es la ausencia de un mecanismo valvular normal en la unión gastroesofágica, lo que permite el escape del contenido gástrico o duodenal hacia el esófago.

Etiología y Patogénesis

Se ha pensando que son muchas las estructuras importantes en la prevención del reflujo. La pinza diafragmática, el ligamento frenico-esofágico y la roseta mucosa fueron considerados entre ellas antes del reconocimiento manométrico del esfínter esofágico inferior (EEI), siendo éste uno de los factores más importantes en la regulación del reflujo. La resección de la unión GE o la miotomía completa de las fibras que separan el EEI conducirá invariablemente a reflujo severo y prolongado.

Se ha comprobado que la presión del EEI es variable, siendo infuenciada por factores de "stress", efectos hormonales, influencias farmacológicas, y probablemente factores emocionales,[1 3] los cuales son muy difíciles de controlar bajo condiciones experimentales.

Se ha sugerido incluso que una disminución de la presión del EEI pueda ser el efecto y no la causa del reflujo. Se demostró que pacientes con síntomas de reflujo pero con endoscopías normales respondían con una elevación normal de la presión del EEI a una dosis de pentagastrina, mientras que en aquéllos que endoscópicamente presentaban esofagitis la respuesa a la pentagastrina estaba abolida.[4 5]

La posibilidad de daño al mecanismo del EEI por el reflujo pone en duda si el defecto primario reside en el EEI o en algún mecanismo como la gastrina [7 9] y la progesterona[10 11] en dosis farmacológicas pueden causar cambios en la presión esfintérica. La importancia de este efecto hormonal en cantidades fisiológicas aún no se ha elucidado.

En adición a las hormonas, existen varios agentes farmacológicos clínicamente importantes que producen un efecto nocivo en la presión del EEI y que por consiguiente pudieran ser importantes en la patogénesis del reflujo GE. Los dos más frecuentemente usados son: el alcohol[12] y el humo de tabaco.[13] Las drogas anticolinérgicas producen una disminución de la presión del EEI,[14] aunque no existe evidencia de que causen reflujo.

Resumiendo la participación del EEI en la patogénesis del reflujo GE podemos afirmar que una disfunción del EEI puede ser demostrada en la mayoría de los pacientes con reflujo, y que esta disfunción puede ser bien la causa o el resultado del reflujo. Es necesario aumentar nuestros conocimientos sobre los sistemas de control del EEI y sus posibles alteraciones antes de lograr entender su patogénesis.

Defensas del Cuerpo del Esófago contra el Reflujo

Una vez el líquido traspasa el EEI y llega al esófago estimula la peristalsis secundaria lo cual ayuda a remover el líquido ofensivo. La presencia de una onda peristálica, empero, no es garantía para que sea devuelto al estómago prontamente. Los pacientes con reflujo sintomático requieren una mayor cantidad de tragos que los pacientes normales para aclarar el ácido del esófago.[15] Existe una buena correlación entre la disminución en la habilidad para aclarar el ácido y los descensos de pH intraesofágico prolongados, especialmente durante el sueño.[16] Esta habilidad para el aclaramiento del ácido en el esófago puede ser de crucial importancia, ya que evaluaciones prolongadas sugieren que todos los individuos tienen pequeños accesos de reflujo,[17 18] pero aquellos con reflujo sintomático tienen ácido en el esófago, por períodos más prolongados, especialmente durante la noche.

Manifestaciones Clínicas y Complicaciones

Los síntomas del reflujo GE están relacionados con el retorno del contenido gástrico al esófago y a la cavidad oral. Los más frecuentes son:

1) *Vómito y regurgitación*: La inmensa mayoría de los infantes presentan el inequívoco síntoma de regurgitación de líquido a la boca, generalmente después de la alimentación. Este es un fenómeno pasajero y se considera sea debido a la

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relativa falta de madurez del sistema del EEI con la consiguiente disminución de la presión. Esta llamada *calasia* suele resolverse por sí misma en la mayoría de los casos durante los primeros seis meses de vida, sin que se hayan demostrado complicaciones futuras. La persistencia del problema invita a una investigación del sistema motor del esófago por los riesgos que pudiera acarrear más tarde.

Cuando un paciente mayor asegura que despierta tosiendo o con la boca llena de líquido implica un grado severo de reflujo.

El vómito o expulsión forzada del contenido gástrico es indicativo de reflujo patológico. El niño suele expulsar el alimento que poco antes ingirió, contrario a lo que ocurre en los síndromes obstructivos del tracto de salida gastroduodenal. Causan mayor alarma aquellos casos en los que el vómito produce episodios de laringoespasmo con dificultad respiratoria y cianosis. Estos en su mayoría son fácilmente diagnosticables por su aparatosa expresión clínica.

2. *Malestar retroesternal ("Heartburn"):* En los niños mayores con facilidad de expresión verbal y en los adultos, la manifestación clínica más frecuente es el malestar retroesternal, comunmente llamado "hervedera". Es ésta una desagradable sensación de quemazón retroesternal, comenzando en el epigastrio y ascendiendo hasta el cuello. Suele ocurrir después de las comidas, al inclinarse el paciente, o en situaciones en que la presión intragástrica aumente superando la presión ejercida por el EEI (maniobra de Valsalva).

3. *Disfagia.* las molestias al tragar suelen aparecer cuando hay esofagitis presente sin que necesariamente tenga que acompañarse de estrecheces esofágicas. Generalmente, la dificultad para tragar es principalmente con los alimentos sólidos y el arresto del bolo alimenticio suele ser transitorio. En adición, el paciente está consciente del tránsito del alimento por el tracto esofágico, pudiendo seguir esta sensación a lo largo del cuello con el dedo.

4. *Hemorragia:* La presencia de sangre es indicativa de esofagitis. El sangramiento es generalmente de naturaleza roja viva o en "borra de café", y no es raro que sea la primera manifestación de esofagitis por reflujo. Ocasionalmente la hemorragia es masiva.

5. *Manifestaciones Pulmonares:* Sibilancias intermitentes, ronquera, "bronquitis" o asma pueden ser las únicas manifestaciones del reflujo GE.[19 20] Con frecuencia aparecen informes en la literatura médica sobre la asociación de asma crónica y reflujo GE. Cuando una de estas entidades clínicas es diagnosticada el reflujo gastroesofágico debe ser incluido en el diagnóstico diferencial.

6. *Detención de Crecimiento (FTT):* Existen tres mecanismos para la aparición de detención del crecimiento en los niños con reflujo GE: 1) la simple pérdida de nutrientes, 2) disfagia, malestar, alteración del sueño, pobre apetito y miseria general causados por la esofagitis, y 3) pérdida endógena de elementos sanguíneos y proteínas. Podemos asumir que en los casos más severos se desarrolla un ciclo consistiendo de incompetencia cardioesofágica, regurgitación de jugo gástrico, esofagitis, ulceración y dilatación del esófago, aumento de la incompetencia del mecanismo de cierre, más regurgitación, etc. Este ciclo puede hacer que el reflujo GE persista después de la infancia y que la estrechez esofágica sea la secuela del mismo.

7) *Síndrome de Muerte Infantil Súbita (SIDS):* Existe evidencia preliminar de que el reflujo pueda ser el causante de SIDS.[21 22 23] Esto se basa en el hecho de que en niños que han estado al borde de la muerte por el antedicho síndrome y han sido resuscitados, la corrección del reflujo ha evitado posteriores problemas. Los hallazgos patológicos (petequias en pulmón y timo, hipertrofia de las arteriolas pulmonares, aumento de la fluidez sanguínea, disminución del pO_2 en el ventrículo izquierdo, eritropoiesis hepática y cambios laríngeos, con necrosis fibroide, edema e inflamación) son por demás consistentes con el hecho de que el laringoespasmo sea el descencadenante de SIDS; y que éste a su vez haya sido iniciado por el reflujo GE.[24]

8. *Presentaciones poco usuales:*

a) *Rumiación* - Consiste en la regurgitación voluntaria de alimentos seguida de movimientos masticatorios, con aparente placer para el niño. En muchas ocasiones el niño acaba malnutrido y en un tiempo la mortalidad por este mecanismo fue de 25-50%.

b. *Síndrome de Sandifer* - Consiste de movimientos bizarros de la cabeza, anemia y esofagitis. En muchos de estos casos se puede demostrar reflujo GE. No existe un mecanismo convincente para explicar el porqué de estos movimientos bizarros.[25 26 27]

c. Herbst identificó varios pacientes con hipoproteinemia, enteropatía con pérdida de proteínas y dedos en palillo de tambor, asociados a reflujo GE. Todos tenían esofagitis severa y la albumina se normalizó luego de la corrección quirúrgica del reflujo.[28]

Diagnóstico

Hay varios exámenes y procedimientos disponibles para la evaluación de la función esofágica. Cada prueba está diseñada para contestar una pregunta específica.

Esofagograma: (Fig. 1) Es el método más usado para determinar la presencia de reflujo. Aún cuando su sensitividad es menor que la de otros estudios, la información que obtenemos de él es sumamente valiosa. La presencia de anormalidades anatómicas del esófago, así como estenosis pilórica, membranas antrales ("webs"), páncreas anular, malrotación, etc., deben ser descartadas como causantes de la sintomatología del paciente.

Fig. 1. Demostración de RGE por medio de Fluoroscopia.—La columna de bario asciende hasta el nivel de la primera costilla en este niño con problemas pulmonares repetidos. El estudio de pH esofágico demostró reflujo de tipo continuo. El tratamiento quirúrgico fue exitoso.

Estudios de pH (Tuttle test) y Manometría: (Fig. 2) El método de perfusión constante para la determinación de las presiones esofágicas y el estudio de pH esofágico son de incorporación reciente al armamentario diagnóstico para la evaluación del reflujo GE. El procedimiento es muy simple: se coloca a través de una sonda nasogástrica una cantidad predeterminada de glucosa al 5% en el estómago, insertándose luego la probeta de pH para determinar el grado de acidez gástrica. La probeta de pH es luego retirada y localizada 5 cm proximal al EEI. El pH esofágico intraluminal es entonces determinado por espacios variables de tiempo (por lo general por una hora). Un descenso de pH por debajo de 4 (normal 6.0 - 7.0) en dos ocasiones es considerado diagnóstico de reflujo GE.[29 30 31]

Los estudios de pH esofágico son considerados por muchos como los más sensitivos y fisiológicos para la determinación de la presencia de reflujo GE.

La manometría no es útil para la determinación de reflujo, pero si es de gran valor para la evaluación fisiopatológica del EEI y del estado motor íntimo del esófago.

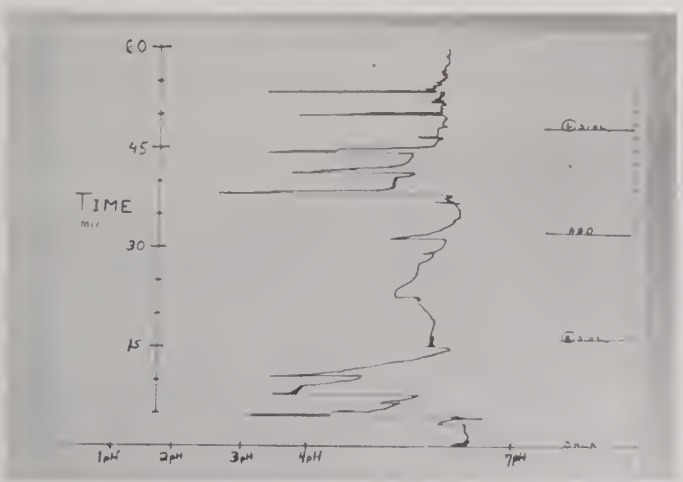

Fig. 2. Estudio de pH en un infante con RGE.—Una vez en el cuerpo del esófago el pH es de 6. A los 5 minutos se registra un descenso precipitado del pH, hecho que se repite sucesivamente durante una hora de estudio.

Reflujo Radioisotópico: (Fig. 3) Esta nueva técnica utiliza una solución que contiene tecnecio coloidal 99^{m} colocada en el estómago y la detección del material refluido con una cámara gamma. En la descripción original de esta técnica, 90% de los pacientes con sintomatología y prueba de pH positivas demostraron reflujo.[32 33]

Fig. 3. Escintigrama Esofágico Positivo.—Después del paciente ingerir microcuris de tecnecio coloidal se puede observar el reflujo del material hacia el área esofágica.

Endoscopía: (Fig. 4) Con el advenimiento de los instrumentos de material flexible es posible llevar a cabo este procedimiento en todo tipo de pacientes, no importa su edad.[34] La esofagoscopía con biopsia de la mucosa esofágica es el método más sencillo y sensitivo para la detección de esofagitis.

Los primeros cambios que se observan en la mucosa consisten en hipertemia y aumento en la friabilidad de la mucosa. En estados más tardíos, se observan lesiones similares a la leucoplasia. Estas placas están rodeadas por un borde hiperémico, tienden a hacerse frecuentes, y a crear erosiones longitudinales. Según el proceso inflamatorio progresa, pueden verse claramente zonas hemorrágicas y denudadas en la mucosa esofágica. Por último, y en estadíos muy avanzados, se pueden observar las estrecheses esofágicas. La incidencia de complicaciones durante el procedimiento es sumamente baja (<1 por mil).[35]

Fig. 4. Esofagoscopia en un niño de 2 meses con Esofagitis por reflujo.—La mucosa esofágica se encuentra erosionada y cubierta por material fibrinoide.

Manejo y Tratamiento

Las guías para el manejo de los pacientes con reflujo GE han adquirido una nueva importancia para el pediatra debido a complicaciones del mismo. La Tabla I resume los principios del manejo médico del reflujo GE.

TABLA I

Manejo del Reflujo Gastroesofágico

- Medidas Físicas
- Medidas Dietéticas
- Medicamentos
- Medidas Quirúrgicas

Los infantes deben ser colocados en una posición elevada a un ángulo de 30 grados.[36 37] La cabecera de la cama debe ser elevada al menos 8 pulgadas, lo que se puede conseguir con bloques de madera o concreto.

Las manipulaciones dietéticas pueden ser un componente importante de la terapia.[38] La alimentación frecuente y en pequeñas cantidades disminuye los episodios de vómito aunque el reflujo clínico inaparente puede persistir. No existe evidencia experimental que apoye el uso de alimentos espesa-

dos en el manejo de estos pacientes.

Las grasas retardan el vaciamiento gástrico y disminuyen la presión del EEI, mientras que las proteínas causan el efecto contrario.

Se ha demostrado que el chocolate, gran favorito de los niños, disminuye la presión del EEI. Se ha hipotetizado que las metil-xantinas que contiene inhiben la fosfodiesterasa. Este agente desactiva el AMP cíclico, el cual relaja el músculo liso y podría tener un efecto similar en el EEI.

Aunque no es conveniente evitar alimentos específicos, la disminución de la grasa y el chocolate en la comida puede ser muy beneficiosa. Además los adolescentes deben ser advertidos sobre los efectos nocivos que sobre la función de EEI tienen el alcohol y el humo de cigarrillo.

Los antiácidos no están indicados en la manejo del reflujo GE, excepto en aquellos casos en que se ha demostrado esofagitis.

Euler et al.[39] recientemente demostraron que el uso de betanecol (Urecholine®), un agente colinérgico, es útil en el manejo de la condición que nos ocupa. Su administración produce un aumento sostenido de la presión del EEI que junto a las medidas antes mencionadas puede ser un arma valiosa en el tratamiento de reflujo gastroesofágico.

Varios tipos de drogas, incluyendo agonistas adrenérgicos, bloqueadores alfa adrenérgicos, inhibidores de la fosfodiesterasa, y anticolinérgicos en grandes dosis, disminuyen la presión del EEI. El isoproterenol y la teofilina tienen un particular interés ya que ambas son usadas en el manejo de asma crónica. Si como la evidencia reciente lo sugiere, el reflujo GE contribuye a enfermedades pulmonares recurrentes, estos agentes podrían complicar aún más el problema al disminuir la presión del EEI.

Finalmente, el concepto de la *"barrera flotante"* ha ganado muchos adeptos. Se piensa que el ácido algínico y el bicarbonato sódico reaccionan en presencia de la saliva, formando una solución altamente viscosa de alginato sódico (pH 5-6) que flota en la superficie del contenido gástrico. La eficacia de esta mezcla, conocida en el mercado como Gaviscon®, está sujeta a estudio.

En general, los infantes, niños y adolescentes con reflujo GE deberán recibir tratamiento médico por un período no menor de 3 meses. Esto es particularmente cierto en aquellos infantes cuyo único problema es el vómito, ya que en la mayoría de los casos se puede esperar una buena respuesta. Por otro lado, aquellos infantes que continúan con retraso en el crecimiento, problemas pulmonares recurrentes y estreches asofágicas, deben ser considerados candidatos para la corrección quirúrgica del reflujo GE.

El tratamiento quirúrgico de elección es la fundoplicación de Nissen.[40] Es una operación excelente, relativamente fácil para el cirujano pediátrico hábil y con muy pocas complicaciones postoperatorias.

Summary: **Gastroesophageal reflux is a common pediatric problem associated with considerable morbidity. The most frequent and severe manifestations are recurrent pulmonary disease and failure to thrive. Several diagnostic modalities are in current use for its early detection, the esophageal pH studies being the most sensitive. Physical and mechanical measures are the cornerstone of therapy. Surgery must be considered in those cases with severe complications.**

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"Doquiera hay sangre española se caracteriza la gran afición al teatro, y es natural que en una población de alrededor de 28,000 almas de esta descendencia se haya incluido un teatro entre sus instituciones. El Teatro de San Juan es una versión abreviada de las casas de drama de Madrid. Consiste de tres plantas, y tiene capacidad para sentar a mil personas".

"En Porto Rico hay solo una compañía teatral organizada y esta divide sus compromisos entre varias ciudades grandes de la Isla, pasando como un mes de cada tres en San Juan. La organización incluye una combinación de drama, opera y trovadores, sostenida además por un circo hipodrómico, una colección de monos, y una banda de toreadores nativos".

Descripción de Don José de Olivares, 1899.

PRESENTACION DE CASOS

Strogyloidiasis In The Immunosuppressed Host

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Abstract: A 29 year old man presented with vague abdominal pains, distension and vomiting 8 months after kidney transplantation. Six day after emergency laparotomy he developed massive pulmonary infiltrates and died. An overwhelming generalized infestation with Strongyloides stercoralis was seen; this was unsuspected, and not detected even at bronchoscopy. Retrospectively, occasional eosinophilia could have been the only alterting sign after transplantation. Subsequently, we have diagnosed and treated successfully three other transplanted patients with Stronghyloides stercoralis suspected on the basis of persistent eosinophilia. With the widespread use of immunosuppressors for kidney transplantation and other conditions, it is suggested that severe Strongyloidiasis and othr parasitoses may appear more frequently, and should enter the suspects' list in acute and chronic illnesses. Eosinophilia in immunosuppressed patients should be carefully studied.

Sepsis continues to be the main cause of death in renal transplant recipients. This is secondary to a variety of factors, the most important of which are the immunosuppressed status of the recipient, the generally poor condition of the uremic patient, and perhaps an altered microbial environment. Pulmonary sepsis is one of the most frequent and pehaps the most dangerous of septic complications in transplant recipients. Most reports deal with bacterial, fungal and viral infections, and parasitic conditions are usually not highlighted.

With the widespread use of immunosuppressors for kidney transplantation and other conditions, and with availability of these services to a larger segment of the population especially in tropical and sub-tropical countries, parasitic conditions should be considered and looked at more carefully.

As an example, we discuss a patient with disseminated Strongyloides stercoralis, who developed fulminant pneumonia with respiratory failure, and who eventually succumbed to this complication.

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Illustrative Case

This 29 year old male patient received a kidney transplant from his mother in May 1977. The early post-transplant course was normal, except for one minor episode of rejection and an acute iritis. Pre-transplant eosinophil count was 10 cells per 100 leukocytes, but the cause of this was never investigated, although stool exam was negative for ova and parasites. Eosinophil count was subsequently normal during succesive admissions, except for a count of 2-6 cells per 100 leukocytes during the admission for iritis.

The patient was admitted eight months after the transplant with evidence of partial intestinal obstruction, was treated with nasogastric suction and diet restriction, and discharged on a soft mechanical diet. Two weeks later, he was readmitted with dehydration, a 15 pound weight loss and mild abdominal distention. An operation was performed for partial intestinal obstruction and adhesions over the jejunum were lysed. A long tube was passed into the small intestine and this required manipulation of the bowel. After surgery, the patient continued with abdominal discomfort and distention. On the 6th post-operative day, he developed rapidly progressive shortness of breath, hypoxemia, and cyanosis. The chest x-ray, which had been normal that morning, showed slight infiltrates within four hours, and massive infiltrates within eight hours after onset of dyspnea. Intubation and respiratory assistance was started. Examination of tracheal washings showed no bacteria, fungi, P. carinii, or other organisms. The patient was treated with massive antibiotics and respiratory and vascular support, rapidly developed coma, disseminated intravascular coagulation, and died 36 hours after the onset of the respiratory failure.

Autopsy showed Strongyloides stercoralis in the small bowel, duodenum, and liver, and the lungs were replete with the organisms. There was massive pulmonary edema, intrapulmonary hemorrhages and infiltrates consisting mostly of polymorphonuclear leukocytes.

Discussion

Infestation with Strongyloides stercoralis is frequent and on occasions endemic to many areas in the world, including Puerto Rico. Massive infestation occurs in undernourished individuals, but is seldom reported to cause symptomatic disease. Since 1966, however, it has been reported with increasing frequency as a significant pathogen in immunosuppressed individuals.[1 2 3 4 5 6]

Rivera et al[5] presented nine cases of strongyloidiasis in patients who had received steroids or other antimetabolite drugs for the treatment of a variety of neoplastic and autoimmune diseases. Eight of the nine patients died and

several of these had presented uncontrolable diarrhea. A severe infection and, in some cases, massive dissemination with Strongyloides stercoralis precipitated the death of the patients. In transplant recipients four previous reports attest to this complication.[7 10]

It becomes clearly evident that a wider use of drugs which alter the immune response either directly, as in the case of immunosuppression for autoimmune disease and transplant recipients, or as a by-product of chemotherapy, as in the case of treatment for cancer, will result in a decrease in the natural host barriers which prevent Strongyloides from invading the host.[2 3]

Because of this, it becomes of critical to detect the presence of this organism early, ideally before immunosuppression is started. Treatment with thiabendazole is curative in the vast majority of circumstances in patients with normal defenses and normal nutrition.[11] However, if infestation is massive, or if the patient is clinically symptomatic and there is dissemination in addition to immunosuppression, then thiabendazole may probably not be effective.

At present, we are investigating all cases of eosinophilia in our program before transplantation. We have not been able to identify any case pre-operatively, but three patients have developed eosinophilia 12, 18 and 24 months respectively after transplantation, and have subsequently shown a positive stool culture for strongyloidiasis. Treatment with thiabendazole has been successful, in spite of continuing immunosuppression. In one of these patients, the syndrome of diarrehea and partial intestinal obstruction was present. Regular stool examination for ova an parasites has a low sensitivity for Strongyloides. However, a stool concentration followed by test-tube incubation at room temperature, results in a higher sensitivity. In the occasional case we still perform duodenal intubation with a nasogastric tube, washings and aspiration, followed by examination of the washings. The use of a duodenal capsule is being studied.

Kidney transplanters and other physicians using chemotherapeutic and immunosuppressive agents, particularly in tropical regions, should be constantly aware of this complication, and every effort should be made to identify the presence of helminths before transplantation. In patients who develop eosinophilia or a picture of non-specific abdominal distress, diarrhea, or partial intestinal obstruction, strongylidiasis should immediately enter the suspect list in the differential diagnosis.

Resumen: **Se discute el caso de un paciente de 29 años que presenta dolor y distensión abdominal, junto con vómitos 8 meses después de un transplante de riñón. Seis días después de una laparotomía exploratoria desarrolla extensos infiltrados pulmonares y fallece. Se comprobó una infestación masiva por Strongylides stercolaris la cual nunca se sospechó. De forma retrospectiva se piensa que la eosinofilia presente pudo haber sido el único signo de alerta luego del transplante. Subsecuentemente hemos diagnosticado y tratado con éxito infecciones por S. stercolaris en otros tres pacientes con transplante de riñón. La sospecha se inició por la precensia de eosinofilia persistente.**

Con el amplio uso de agentes inmunosupresores en transplantes de órganos y otras situaciones se ha sugerido que las infecciones por S. stercolaris y otros parásitos ocurren con una frecuencia mayor de lo sospechado y deben tenerse en mente en estos pacientes con enfermedades crónicas y agudas. La eosinofilia en el paciente inmunosuprimido debe ser más extensamente estudiada.

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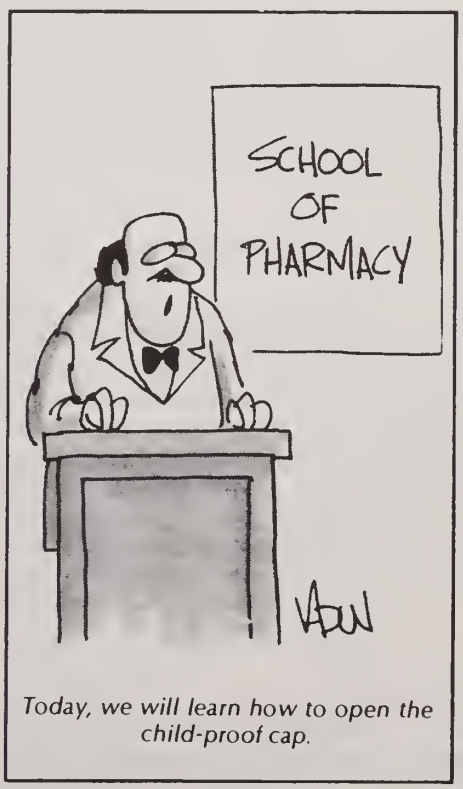

Today, we will learn how to open the child-proof cap.

Delayed Presentation Of A Congenital Diaphragmatic Hernia Resulting In Stomach Incarceration

Manuel E. Lores, MD
Rubén Delgado, MD
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Summary: **We report a 5-year-old girl with a normal chest x-ray early in life who presented with stomach incarceration within the left hemithorax through a congenital posterolateral diaphragmatic hernia. In patients with late appearance of congenital diaphragmatic hernia there is no respiratory compromise and the clinical picture is related to mechanical obstruction of the portion of the gastrointestinal tract herniated through the diaphragmatic defect.**

The posterolateral diaphragmatic congenital hernia is the most common and serious developmental anomaly of the diaphragm. There is incomplete closure, or no closure of all, of the pleuroperitoneal hiatus (foramen of Bochdalek) in the posterolateral aspect of the diaphragm through which the bowel herniates into the chest. With growth of the gut and the other abdominal viscera which may have herniated into the chest, the developing lung is compressed and the abdomen loses much of its stimulus to enlarge. This compromise in the growth and development of the lung will cause pulmonary hypoplasia which is directly proportional to the degree of lung compression and is the single most important factor detrmining the prognosis in these infants. Usually the newborn presents with severe respiratory distress requiring emergency measures and surgical treatment. However, occasionally the lung is not markedly compromised, there are no early symptoms and the diagnosis might be delayed for several years.

Case Report

A 5-year-old girl was hospitalized with persistent left lower chest and upper abdominal pain associated with nausea and vomiting 48 hours after a sustained respiratory effort during swimming lessons. Past medical history was essentially negative except for the usual childhood diseases. Positive findings on physical examination included moderate dehydration, decreased breath sounds in the left hemithorax plus epigastric and left upper abdominal tenderness to palpation. A chest x-ray on admission showed elevation of the left hemidiaphragm. (Fig. 1) A previos chest film taken at 3 years of age was normal. Intravenous fluids and nasogastric tube

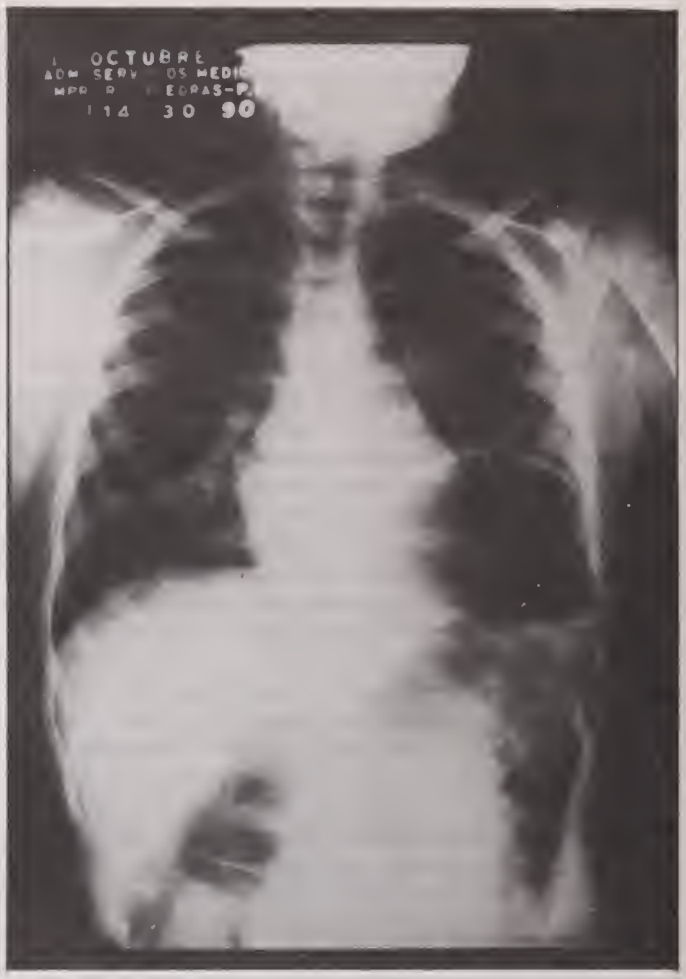

Fig. 1: Chest film done at admission to the Hospital. Elevation of the left hemidiaphragm can be clearly seen.

suction were started. Despite adequate gastric decompression the patient continued with persistent nausea, vomiting and pain. In view of this, a contrast roentgenographic study of the stomach was performed injecting gastrographin solution through the nasogastric tube. This study demostrated mechanical obstruction of the stomach within the left hemithorax (Fig. 2). An emergency laparotomy was then done through an upper abdominal midline incision. The fundus and body of the stomach were found to be herniated and incarcerated into the chest through a typical posterolateral diaphragmatic defect with smooth margins measuring 4 x 3 cm. There was no traumatic tear in the diaphragm and no hernia sac. Rotation of the gut was normal. The stomach was then reduced into the abdominal cavity and its circulation was found to be adequate. The left lung was normal and expanded without difficulty. The diaphragmatic defect was closed and the residual air was aspirated from the left hemithorax. The postoperative course was uneventful and the patient was discharged during the fifth postoperative day.

Discussion

The case reported here is a classical example of a congenital left posterolateral diaphragmatic hernia appearing late in childhood. This patient had an unremarkable past

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history including a normal chest x-ray at 3 years of age. In this patient, although the diaphragmatic defect was congenital, the visceral herniation did not occur until late in childhood and thre was no compromise with the normal growth and development of the lungs. These patients should be expected

Fig. 2: Contrast study of the stomach showing mechanical obstruction within the left hemithorax.

to have normal pulmonary function and it is rare for them to present with respiratory symptoms. Most commonly they present with gastro-intestinal symptoms related to mechanical obstruction of the bowel segment herniated through the diaphragmatic defect.[1 2 3] It has been suggested that the most important factor predisposing to herniation in these patients is related to sudden and significant pressure changes in the thoracoabdominal cavities.[1 3] In the case presented here it is reasonable to postulate that a significant increase in the intra-abdominal pressure secondary to a severe respiratory effort while swimming caused the narrow diaphragmatic defect to widen and the stomach to herniate into the chest.

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Variety of Ills Can Cause Earache

Earache Hits Many

There are many causes for pain in the ear.

One of the most common, particularly in summer, is an infection of the outer ear caused by swimming in contaminated water. This earache often is called "swimmer's ear." Symptoms are pain (particularly when the ear is pulled), itching and discharge. Medical attention is required.

Earaches in the middle ear often follow respiratory infections. Germs in the nose and mouth move into the middle ear. Children are particularly susceptible to middle ear infections. Infected tonsils also can cause a middle ear infection. An infant with ear infection cries loudly, particularly when lying down, pulls or bats at his ear, or turns his head from side to side.

Medical attention is required for all middle ear infections. Do not put cotton swabs, hairpins, matches or anything else in the ear.

Children often put objects into their ears. these might be peas, beans, beads, paper or cotton. Insects also may get trapped inside the ear.

If the insect is alive and buzzing, put several drops of warm oil (baby, mineral or olive oil) into the ear to kill the insect. this is the only time putting oil into the ear is justified. Go to the doctor to have the insect removed. Other small objects trapped inside the ear also need medical attention for removal. The only possible exception is paper or cotton, if it is clearly visible outside the ear canal. One attempt to remove it may be carefully made with tweezers. See a doctor to make certain all of it has been removed.

The American Medical Association's Handbook of First Aid and Emergency Care cautions: Do not put water or oil into the ears to attempt to flush out the object. This may cause the object to swell and make removal even more difficult.

Bleeding from the ear is a medical emergency. Do not try to stop the flow of blood. Cover the ear loosely with a bandage or cloth to catch the flow of blood and go promptly to the doctor or hospital emergency room.

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Frank Chappell
Science News Editor
AMA

WORD HEALTH ORGANIZATION / ISFC INTERNATIONAL SOCIETY AND FEDERATION OF CARDIOLOGY

ARTICULOS ESPECIALES

*Definición y Clasificación de las Miocardiopatías**

A continuación el informe del proyecto conjunto entre la Organización Mundial de la Salud (OMS) y la Sociedad Internacional y Federación de Cardiología (ISFC) para la definición y clasificación de las miocardiopatías.

Por la diversidad de términos, conceptos, y definiciones utilizados para describir y clasificar estos trastornos cardíacos consideramos este informe de importancia tal que merece ser publicado para el conocimiento de nuestros lectores.

I. **Definición**

Las miocardiopatías son: "enfermedades del músculo cardíaco de origen desconocido".

II. **Clasificación**

A. Miocardiopatía con Dilatación ("Dilated Cardiomyopathy").

Esta condición se reconoce por la dilatación de uno o ambos ventrículos. La dilatación es frecuentemente severa y se acompaña de hipertrofia ventricular. La función ventricular está afectada y puede o no ocurrir fallo cardíaco congestivo. En ocasiones se acompaña de disritmias que pueden ser atriales o ventriculares y tener consecuencias fatales.

B. Miocardiopatía Hipertrófica**

Se caracteriza por una hipertrofia desproporcionada del ventrículo izquierdo (y ocasionalmente del derecho) que típicamente envuelve más el septo interventricular que a la pared del ventrículo, pero que puede ser concéntrica ocasionalmente. El volumen ventricular izquierdo está normal o disminuido y la presencia de gradientes sistólicos es frecuente. Se han descrito una serie de características morfológicas en esta entidad siendo más marcadas en el septo.

Este tipo de miocardiopatía se transmite de una forma autosómica dominante con penetrancia genética incompleta.

C. Miocardiopatía Restrictiva

Puede existir con o sin obliteración de las cavidades. La miocardiopatía restrictiva incluye la *fibrosis endomiocardiaca* y la *miocardiopatía de Loffler.* Se propone que a esta condición se le denomine: *endomiocardiopatía eosinofílica.* La formación de tejido cicatricial endomiocardiaco usualmente afecta uno o ambos ventrículos y restringe su llenado. El envolvimiento valvular atrio-ventricular es común pero los tractos de salida no se afectan. La obliteración cavitaria es característica de los casos avanzados.

Hay algunas miocardiopatías que no pueden ser incluídas en ninguno de los grupos antes mencionados. Son casos con alteraciones de menor grado que pueden o no evolucionar a una miocardiopatía franca. A éstos se les ha denominado *miocardiopatía latente:*

III. **Miocardiopatías Específicas**

Son enfermedades del músculo cardíaco de etiología conocida o asociadas a trastornos de otros sistemas.

Se han excluído las alteraciones del miocardio ocasionadas por:

—hipertensión arterial
—hipertensión pulmonar
—enfermedad coronaria
—valvulopatías
—cardiopatías congénitas

Se pensó que la extensión de la clasificación para incluir estas condiciones ampliaría tanto su espectro que le restaría todo su valor.

Estas miocardiopatías específicas se clasifican en:

A. Infecciosas

Estas pueden ser:

1. Virales
2. Bacterianas
3. Por Rickettsias
4. Micóticas
5. Protozoarias (Enfermedad de Chagas)
6. Metazoarias (Filaria)

B. Metabólicas

1. Endocrinas —se incluye la tirotoxicosis, el hipotiroidismo, la insuficiencia adrenal, el feocromocitoma, y la acromegalia.
2. Las tesaurismosis familiares e infiltrados —aquí se

* Recopilado de Heart Beat, Organo Oficial de la Sociedad Internacional y Federación de Cardiología. 1981, Núm. 2, Ginebra, Suiza.

** Previamente conocida como:
—Estenosis hipertrófica sub-aórtica idiopática (IHSS)
—Estenosis sub-aórtica muscular
—Miocardiopatía obstructiva hipertrófica (HOCM)
—Hipertrofia asimétrica
—Hipertrofia septal asimétrica (ASH)

incluyen la hemocromatosis, la enfermedad de Pompe, síndrome de Hurler, y las enfermedades de Niemann-Pick, Hand-Schuller-Christian, Fabry-Anderson y Morquio-Ullrich.

3. Por deficiencia —por trastornos en el metabolismo de potasio, de magnesio, y trastornos nutricionales como el Kwashiokor, la anemia y el beri-beri.
4. Las amiliodosis —incluyen las amiloidosis primaria, la secundaria, las amiloidosis familiares, y la amiloidosis senil.

C. Enfermedades Sistemáticas
1. Trastornos del tejido conjuntivo: lupus eritematoso sistémico, poliarteritis nodosa, artritis reumatoidea, ecleroderma, y dermatomiositis.
2. Infiltrados y Granulomas: Sarcoidosis y leucemia.

D. Heredofamiliares
1. Distrofias musculares: enfermedad de Duchenne; y la distrofia miotónica.
2. Trastornos neuromusculares: Ataxia de Freidreich

E. Reacciones tóxicas y de sensitividad

Aquí se incluyen las miocardiopatías como reacción a: sulfonamidas, penicilina, antimonio, cobalto, emetrina, alcohol, isoprenalina, antiacidinas e irradiación.

La mayoría de las miocardiopatías específicas se asocian con dilatación ventricular aunque hay muchas excepciones. También los infiltrados localizados pueden ocasionar trastornos de conducción y disritmias sin que haya una disfunción miocárdica generalizada.

El informe también menciona brevemente otras miocardiopatías específicas como:

Miocardiopatía alcohólica —en la actualidad no puede precisarse si el alcohol es un agente causal o uno predisponente a esta miocardiopatía.

Miocardiopatía por toxinas —algunas toxinas tienen un impacto sobre el miocardio como en la enfermedad cardíaca carcinoide y como respuesta a la metisergida que también afecta las válvulas.

La miocardiopatía del periparto es un grupo heterogéneo donde el trastorno cardíaco puede manifestarse incialmente poco tiempo antes o después del parto.

Hay ciertos trastornos heredofamiliares como el Síndrome de Noonan y la lentiginosis que pueden producir cuadros idénticos a una miocardiopatía hipertrófica. También, hay ciertos trastornos que no pueden "acomodarse" en ninguno de los grupos mencionados y se incluyen como miocardiopatías no clasificadas. Ejemplos de estas son la fibroelastosis del endocardio, la miocardiopatía infantil histiocitoide, y la miocarditis de Fiedler.

Alcoholism Now Held To Be Serious Ill

Alcoholic Is Sick

In recent years people have been changing their minds about alcoholics.

In the past, they were condemned and rejected. Now there is an earnest desire to help rather than disregard or punish. People are coming to realize that the alcoholic should no more be ridiculed than the cerebral palsy victim. They are recognizing alcoholism for what it is — a serious and tragic disease, a major health problem.

A pamphlet from the American Medical Association points out that the physician today sees the alcoholic as a sick person with an illness that has many sides and consequences. A remarkable upsurge in medical research is in progress. Intensive treatment centers for alcoholic patients are springing up across the country. An increasing number of general hospitals are admitting patients with conditions diagnosed as alcoholism and giving them care.

The American Medical Association and the World Health Organization, as well as many other professional groups, regard alcoholism as a disease. The judiciary and lawmakers also are recognizing it as a disease.

The alcoholic usually drinks heavily and gets drunk often. But quantity and frequency are only one sign. Some alcoholics actually drink less over a given length of time than some social drinkers, but this does not alter the basic condition or make it less serious. The key factor is loss of control and craving for the drug alcohol.

Physical disabilities and difficulties in adjusting to life may contribute to the development of the illness, as well as result from it. Drinking by one's self and drinking in the morning may be signs of alcoholism.

Living on skid row, being irresponsible, and exhibiting other socially unacceptable behavior are not necessarily a part of alcoholism. In fact, alcoholics who are financially successful professional persons are numerous and constitute one of the most seriously neglected groups of problem drinkers in this country.

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Consideraciones Eticas en el Tratamiento de Adolescentes con Gonorrea

J. Silber, M.D., MASS

Resumen: En forma creciente los adolescentes consultan al médico para ser tratados por sus enfermedades venéreas. A menudo surge la pregunta: ¿no deberían saber los padres lo que les está sucediendo? Esta situación a menudo se expresa en términos de conflicto en relación al consentimiento para tratamiento y aseguramiento de confidencialidad.

La forma en que contestamos la pregunta depende de cómo cada sociedad define a los niños en relación a sus padres.

Históricamente la respuesta más temprana fue la doctrina de "patria potestad", que significa que los padres son dueños de sus hijos. Hacia fines del siglo XIX, el estado impuso límites a esa posición en aquellas circunstancias en que se consideraba que los niños estaban en peligro: una posición de "bienestar social". A pesar de la disimilitud entre ambas interpretaciones tiene un elemento en común: los adolescentes no tienen derechos propios.

En las últimas dos décadas surgió una nueva filosofía que se ocupó de los "derechos civiles" de los adolescentes. Este enfoque sólo dá permiso a los padres o al estado a representar al menor siempre y cuando éste no esté en condiciones de hacerlo. Este concepto ha recibido el nombre de la "doctrina del menor maduro". La justificación ética de dicha doctrina está basada en los principios de autonomía y de beneficencia. Las implicaciones legales de estas consideraciones éticas con respecto al tratamiento de las enfermedades venéreas de los adolescentes han sido desarrolladas en las legislaciones estatales promoviendo la atención confidencial.

La gonorrea figura en primer término ente las enfermedades infectocontagiosas de denuncia obligatoria en los Estados Unidos. El número de infecciones que realmente ocurren excede los casos reportados por un margen estimado en 1.6 a 2 millones de casos anuales. La tasa de gonorrea por grupos etareos muestra que los adultos jóvenes y los adolescentes constituyen el grupo de riesgo más elevado para la adquisición de la enfermedad. En 1977 los adolescentes eran el 25% del número de casos de gonorrea reportados[1]. Las consecuencias e implicaciones de la gonorrea en la adolescencia es un área de gran preocupación para todos los que trabajan con la juventud[2]. Este artículo se ocupa de un tema particular y crucial: las consideraciones éticas relacionadas a la atención médica de los adolescentes que consultan para tratamiento de su gonorrea.

El Problema

Cuando un joven concurre a la consulta médica para tratamiento de su enfermedad venérea, sólo o acompañado por sus padres, él se convierte en el paciente y, si la responsabilidad por su atención médica es aceptada, incurrimos en una obligación con respecto a él[3]. ¿Cómo podemos reconciliar nuestra obligación con respecto al joven por una parte y con sus padres por la otra? Este problema puede ser conceptualizado mejor en relación a los términos de consentimiento y confidencialidad.

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Consentimiento y Confidencialidad

El consentimiento es un contrato entre el paciente y el médico.

El médico debe explicar la naturaleza del tratamiento propuesto así como las alternativas existentes a dicho tratamiento, a cambio de lo cual el paciente le dará el permiso para el tratamiento. Y es aquí donde emerge el conflicto: en el caso del adolescente, ni niño ni adulto ¿quién debería dar el consentimiento.

La confidencialidad se ocupa de la naturaleza privilegiada de la información dada al médico por el joven. De acuerdo con esta noción la anamnesis y los hallazgos del examen físico no pueden ser compartidos con otros, incluso sus padres, sin el permiso del joven. De acuerdo con esta noción, pues, surge un conflicto cuando un adoelscente que vive en casa de sus padres adquiere gonorrea, lo que coloca su salud en peligro, y niega a sus padres el derecho de ser informados. ¿No tienen acaso los padres el derecho de ser informados? Esta situación es todavía más complicada en el caso de la adolescente porque pueden estar envueltos otros problemas de índole legal.

¿Cómo define la sociedad al adolescente en relación a sus padres?

La forma en que contestamos la pregunta precedente depende en cierto grado de cómo nuestra propia sociedad define a los niños en relación a sus padres. La respuesta a este tema ha sido variada[4]. Históricamente, la primera respuesta consistió en negar todo derecho a los jóvenes. Los adolescentes por lo tanto no podían consentir su propio tratamiento médico. Esto estaba basado en el contexto de "Patria Potestad", que implica el derecho de los padres a ser dueños de sus hijos. Esta idea todavía tiene vigencia y es visible en decisiones judiciales sobre custodia y adopción. Relativamente reciente, a fines del siglo XIX, fue la imposición de límites al ejercicio de la patria potestad en aquellas circunstancias en que se estimaba que los niños se hallaban en peligro. Esta posición es reconocida como la supremacía del bienestar social. Es claramente identificable en las leyes de enseñanza obligatoria y en las leyes de protección al menor[5] y se aplica a los casos en que los adolescentes adquieren gonorrea como resultado de abuso sexual o de incesto.

A pesar de su disimilitud ambas interpretaciones tienen un elemento en común: los adolescentes no tienen derechos propios y son los padres o el Estado los que determinan lo que corresponde a su mejor interés.

Un grave defecto de la doctrina de patria potestad y de la posición de bienestar social es que ninguna de las dos permite distinguir entre la etapa de dependencia absoluta tan caractertística de la niñez y la etapa de emergente autonomía en el adolescente que se está desarrollando.

En las últimas dos décadas apareció una nueva filosofía que se ocupó del tema de los "derechos civiles" de los adolescentes. Este enfoque permite a los padres y al Estado

representar a un menor solamente durante el tiempo que dicho menor no es capaz de representarse a sí mismo. Como corolario propone lo siguiente: que el nivel de madurez alcanzado por el adolescente sea determinante de la capacidad de dar consentimiento por parte del adolescente, en lugar de disposición legal arbitraria. Este concepto ha recibido el nombre "la doctrina del menor maduro" y está ejemplificada en recientes disposiciones otorgando el derecho a la libertad de expresión en las escuelas y el derecho de los menores a obtener contraceptivos. La doctrina del *menor maduro* ha sido congruente con el punto de vista de pediatras y especialistas en el desarrollo infantil y el concepto ha sido aceptado por la Academia Americana de Pediatría[6]. Se trata de una definición social que reconoce los cambios que coinciden con la creciente capacidad de los adolescentes y que afirma que ellos pueden tomar decisiones racionales y que por lo tanto son competentes para dar consentimiento para su atención médica[7].

La justificación ética en favor de esta posición está basada en dos principios:

1. El Principio de Autonomía: que dice que toda persona debe tener voz y voto en toda disposición con respecto a ella,

2. El Principio de Beneficencia: que dice que siempre que sea posible hacerle un bien a otra persona debe hacerse, o, al menos, que no deben alzarse barreras para impedir la obtención de dicho beneficio.

El principio de autonomía, aplicado al adolescente sufriendo gonorrea, rechaza la noción de que el consentimiento de los padres es un requisito previo a su atención médica y que esto significa un acto de protección. Todo lo contrario, considera la insistencia en el consentimiento paternal como una negación de los derechos del adolescente como persona separada de sus padres.

El principio de beneficencia también brinda claro apoyo a la doctrina del menor maduro: muchos adolescentes que necesitan tratamiento para su gonorrea jamás consultarían al médico si éste insistiera en obtener permiso de los padres previo al tratamiento[8]. Bajo este mismo principio es también fácil ver cómo la confidencialidad de la información que el adolescente comparte con el médico debe ser respetada y que esto está moralmente justificado; la falta de confidencialidad constituirá una barrera a la atención médica.

Discusión.

Ha sido argumentado que los padres tienen derecho a la información completa sobre la condición de salud de sus hijos. También ha sido cuestionado si al invocar el derecho del adolescente a dar el consentimiento para su tratamiento, uno no estaría dando demasiado poder al médico. Estas preocupaciones pueden ser incorporadas en otra pregunta: ¿puede un joven, dependiente de sus padres en todas las esferas, ser considerado independiente en relación al diagnóstico y tratamiento de su enfermedad venérea?

En respuesta a esto debe hacerse constar primero que la eliminación del consentimiento por, o la notificación a los padres no significa que la participación de éstos en la atención de salud de los adolescentes no sea importante; por el contrario, constituye un ingrediente esencial en la atención óptima de la salud del adolescente[9]. El médico en realidad nunca está en posición de adversario con respecto a los padres cuando obtiene el consentimiento del adolescente y mantiene la confidencialidad de la relación médico-paciente (aunque algunos padres puedan percibirlo así). La realidad es que el médico persigue el mismo fin que la familia del adolescente: protegerlo y restaurar su salud.

En la vida cotidiana, a menudo son los médicos quienes aconsejan a sus pacientes adolescentes a que se comuniquen con sus padres, frecuentemente actuando como intermediarios en situaciones de crisis y ayudando a restaurar la organización de la familia. Tampoco hay duda alguna que el médico valora la vida por encima de la confidencialidad y que ésta será sacrificada en casos de peligro, por ejemplo cuando un joven requiere atención por gonoccemia generalizada y rehusa la hospitalización, sin embargo, cuando debe tomarse una medida tan poco usual es obligación del médico el informar a su paciente de que va a hacerse caso omiso de la confidencia y a su vez la razón de esta discusión.

¿Cuáles son las implicaciones legales de éstas consideraciones éticas? Esto, obviamente es del dominio de las legislaciones locales. En la mayoría de los estados norteamericanos, la doctrina del menor maduro está tácitamente aceptada, dado que poseen leyes, estableciendo que los menores pueden dar consentimiento para su tratamiento bajo ciertas condiciones específicas como ser la sospecha de enfermedades venéreas o de embarazo. Además, existen leyes que van aún más allá, creando la categoría de "menor emancipado". Según los estados, caben dentro de esa categoría quienes "viven en domicilio distinto a sus padres", "mantienen un hijo", "son miembros de las fuerzas armadas", etc. Este principio ha sido puesto a prueba en un caso[10]. Debra Carter, de 17 años de edad, había consentido a tratamiento médico sin el conocimiento de sus padres. A pesar de un buen resultado médico, los padres iniciaron juicio al médico considerando que la paciente era una menor de edad y por lo tanto no estaba autorizada a consentir su tratamiento y que por ende había recibido tratamiento médico sin consentimiento válido. Ellos perdieron la disputa. El tribunal decidió que la ley del estado protegía al médico tratante con respecto a ese tipo de litigio; la misma disposición fue confirmada cuando el caso fue apelado.

Desde el punto de vista de potenciales juicios de malapráctica médica , esto significa que actualmente se requiere de todo médico que conozca las condiciones y circunstancias bajo las cuales le está permitido atender adolescentes sin el permiso de los padres, así como qué constituye un menor emancipado en su jurisdicción. Todo esto debe documentarse en la historia clínica. Es de interés hacer notar que hay en vigencia legislación que protege a médicos y a centros de atención médica de ser culpados por aceptar el consentimiento de un menor de buena fe. Así, por ejemplo, si un menor dá falso testimonio con respecto a su grado de independencia eso no invalida el consentimiento aceptado por el médico en buena fe.

La situación jurídica en Puerto Rico está claramente expresada en la Ley Núm. 23 del 19 de mayo de 1975 que releva de responsabilidad civil al médico que ofrezca tratamiento a un menor que ha contraído gonorrea.

Es obvio que el debate alrededor de los derechos del adolescente a dar consentimiento y exigir confidencialidad es sólo un componente de una batalla dentro de las guerras en que la filosofía moral se encuentra envuelta. Nuestra sociedad se haya frente a la encrucijada de un número de diferentes sistemas éticos. Cada uno es el portador de una tradición moral altamente diferenciada, como lo demuestra la aparición de conceptos tan diferentes como ser "patria potestad", "bienestar social" y "derechos civiles". Por cierto cuando dichas tradiciones morales se encuentran, resultan heridas y fragmentadas en el proceso. Por lo tanto no es sorprendente que las

confusiones del pluralismo se expresen con frecuencia en temas que se relacionan con el status de los adolescentes. Aunque dicha confusión está siendo disipada por guías y regulaciones legales, lo que se requiere por encima de todo es la reflexión consciente de todos nosotros.

Abstract

Adolescents increasingly come to physicians' offices for treatment of venereal diseases. The question often arises: "Shouldn't the parents know?" This is frequently expressed in terms of conflict around the issues of consent and confidentiality.

The way in which we answer the preceding question depends on how a society defines children in relationship to their parents. Historically, the earliest response was the doctrine of "parental sovereignty", which assumes a parental claim of ownership of their children. In the late 19th century the state imposed limits to parental ownership in those circumstances in which the children were considered to be in danger: the "child welfare" position. In spite of their dissimilarity, both of these interpretations have a significant element in common: adolescents have no rights of their own. Either the parents or the state determine what is to be in their best interest.

In the past two decades, a new philosophy appeared dealing with the "civil rights" of adolescents. This approach allows for parents or the state to represent the minors' interest only as long as the adolescent is not able to do so. This concept has been referred to as the "mature minor doctrine." The ethical justification for this position is based on the principle of autonomy and the principle of beneficence. The legal implications of this ethical consideration are being developed in state laws which recognize that teenagers should have access to confidential medical care in order to facilitate treatment and control of gonorrhea.

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Obesity Is Major Nutrition Problem

Many Are Too Heavy

During the long and active period of adulthood, people experiment with many new foods and food combinations. Although there is no single *right* way of eating, the foods selected should add up to a diet that provides all the nutrients needed for good health.

The most common nutrition problem of adults in the U.S. is obesity, says a pamphlet from the American Medical Association. Another common problem is iron deficiency in women of childbearing age. Protein and vitamin deficiencies are uncommon; when they occur, they are usually secondary to other problems, such as alcoholism, other serious or chronic illness, a very unusual diet, or inadequate income.

Some people have the conviction that their health depends on an array of supplements — vitamins, minerals, protein, lecithin, and so on. With the thousands of supplements on the market today, however, it is far more difficult to make safe and rational decisions about supplements than it is to plan an adequate diet from ordinary foods.

For those individuals who want to lose weight, the diet should be as normal as possible. Foods should be chosen from each of the four food groups, but the choices can be modified somewhat to reduce total calories. This means using low-fat or non-fat dairy products instead of whole milk; leaner cuts and smaller servings of meats; the minimum number of recommended servings of breads and cereals; and fruits and vegetables without syrups and sauces. It does not mean eliminating any of these important foods.

The four food groups are: Milk group; Meat group; Vegetable-fruit group; Bread-Cereal group.

Adults in their twenties should take a realistic look at their diet and exercise patterns. After high school or college years are over, there may be fewer athletic activities, dances and other activities to justify a high calorie intake.

There is no diet that can bring about physical fitness in a person who is not physically active. For good health throughout adulthood, the best approach is through weight control, an adequate diet and regular exercise.

December, 1980
Frank Chappell
Science News Editor
AMA

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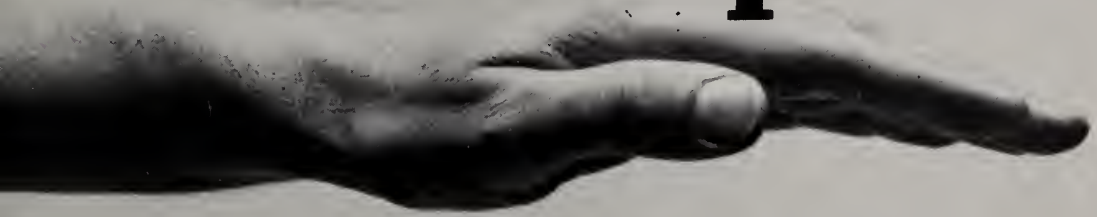

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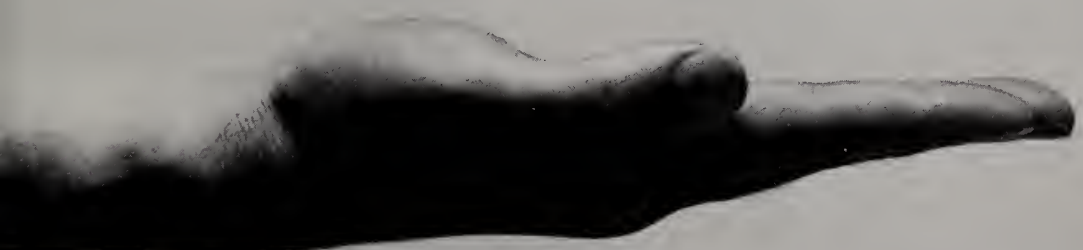

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J-9043-4 July 1981

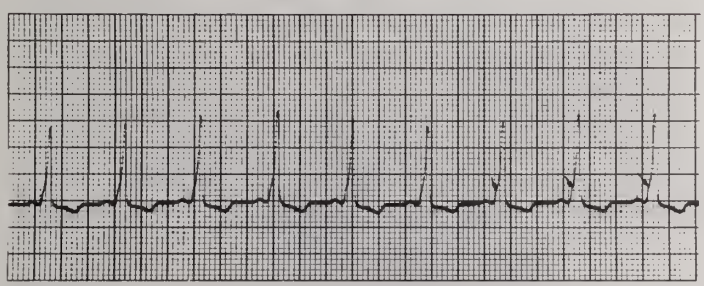
Sección de Autoevaluación

Rafael Villavicencio, MD

ELECTROCARDIOGRAFIA PEDIATRICA

FSO es un niño de 7 años referido para la evaluación de "palpitaciones" de aparición reciente, súbitas, y en reposo. Son de corta duración y no se acompañan de dolor precordial, mareos, ni síncope.

El historial médico pasado del niño es negativo, su examen físico es normal al igual que la radiografía de tórax. La derivación II del electrocardiograma (ECG) que se tomó se ilustra a continuación:



El diagnóstico electrocardiográfico correcto es:

a) bloqueo atrio-ventricular
b) taquicardia ventricular
c) bloqueo de rama
d) síndrome de pre-excitación (Wolff-Parkinson-White)
c) miocarditis

Respuesta

d) Síndrome de pre-excitación

El síndrome de Wolff-Parkinson-White (WPW) es uno de los síndromes de pre-excitación (SPE). En ellos lo que ocurre es que la activación ventricular del estímulo que proviene del atrio ocurre más temprano que cuando éste sigue las vías de conducción A-V usuales[1]. Esto es debido a la presencia de un tracto atrio-ventricular accesorio.

Además de presentar unos cambios electrocardiográficos típicos, los pacientes con esta condición pueden padecer de arritmias severas, en ocasiones fatales.

La verdadera incidencia del SPE en niños no se conoce con certeza, pues éste es un diagnóstico puramente electrocardiográfico y el ECG es un procedimiento que no se hace rutinariamente en pediatría.

En los niños la pre-excitación puede ser transitoria y desaparecer después del año de edad o permanecer intermitente. Ambos factores dificultan aún más la determinación de su verdadera incidencia en la edad pediátrica.

Estudios recientes informan una incidencia de WPW en niños de un 0.15%, con una incidencia mayor en niños con cardiopatías congénitas[2]. El WPW es más frecuente en varones (2:1) que en niñas, y este síndrome puede ser hereditario.

El 50% de los niños con SPE desarrollan taquicardia supraventricular (TSV). La frecuencia de esta complicación es más o menos igual que en los niños con alguna cardiopatía congénita asociada.

La edad en que aparece el primer episodio de TSV es importante, pues se acepta que si esto ocurre antes de los 4 meses de edad, las racaídas son raras, y si ocurren son de corta duración. Cuando el episodio inicial ocurre más tarde, las recaídas son más probables y frecuentes.

Criterios Diagnósticos

1) El intervalo PR es anormalmente corto para su frecuencia cardíaca y su edad. No todas las derivaciones electrocardiográficas demuestran un PR corto.
2) Intervalo QRS prolongado
3) Onda delta - es un "empastamiento" que puede apreciarse en la parte inferior de la onda R del complejo QRS. Esta onda se produce por la activación ventricular temprana através del tracto accesorio (Kent en WPW). Más tarde la activación através del haz de His producirá el resto del QRS en el ECG.
4) Según la configuración del QRS en las derivaciones precordiales, el WPW se ha clasificado en 3 tipos:
   a) tipo A: el QRS simula patrón de bloqueo de rama derecha y una onda delta positiva en los precordiales derechos.
   b) tipo B: el QRS parece bloqueo de rama izquierda con una onda delta positiva en V_6.
   c) tipo C: ondas delta y complejo QRS positivo en todo el trazado electrocardiográfico.

El más común es el tipo B con una incidencia aproximada de 66%. Le siguen los tipos A y C con incidencia de 28% y 10.5% respectivamente en las series de Gillette y Garson recientemente reportadas[3].

Análisis del Trazado

En el caso presentado se aprecia un ritmo regular, con una frecuencia ventricular de 110/minuto. El intervalo PR es de 0.08 sec. y la duración del QRS es de 0.10 sec. En la porción ascendente del QRS puede apreciarse el empastamiento inicial que es la onda *delta.*

Mecanismo

Se ha aceptado que el síndrome de WPW ocurre debido a una pre-excitación ventricular através de un tracto de conducción accesorio (TCA) o haz de Kent, que se origina en el atrio y termina en el miocardio ventricular. Por ello, parte, o todo el ventrículo se activa antes de que se depolarize el haz de His.

La explicación de las taquicardias en estos pacientes está basada en la formación de un ciclo compuesto de: atrio —nodo atrioventricular— ventrículo, y el tracto accesorio. Es esencial para el comienzo de este ciclo el que exista un bloqueo unidireccional en una de las dos vías atrio-ventriculares seguido de conducción-ventricular por la otra vía.

Muchas veces un prematuro atrial (PA) es el desencadenante de las taquicardias. En estos casos lo que ocurre es que el PA es bloqueado en el tracto accesorio y se conduce exclusivamente al ventrículo através del nodo A-V. Luego de la excitación ventricular hay una re-excitación atrial através del tracto accesorio. Al perpetuarse este movimiento es que resulta la taquicardia.

Se ha mencionado que los ecos atriales y ventriculares son otros mecanismos capaces de iniciar una taquicardia en este síndrome.

Situaciones Clínicas

El WPW puede ocurrir en niños con corazones anatómicamente normales, sin embargo la incidencia de taquidisritmias es mayor en aquellos donde hay una cardiopatía congénita asociada. Las cardiopatías más frecuentes en estos casos son:

1) enfermedad de Ebstein de la válvula tricuspídea.
2) inversión ventricular
3) prolapso de la válvula mitral
4) miocardiopatías

Historia Natural

Puede desaparecer espontáneamente, en la mayoría de estos casos se ha postulado que la solución de las disritmias y el SPE ocurre debido a una "maduración" del sistema de conducción, al desarrollo de la inervación adrenérgica, y a una disminución de la dominancia colinérgica.

En los estudios del grupo de Texas[3] se documentaron los siguientes resultados con relación a la "historia natural" del WPW:

1) desaparición de hallazgos en el ECG (29%)
2) 70% de los casos en que desapareció el WPW también cesó la TSV.
3) En los casos en que el WPW persistía, 40% de ellos dejaron de tener TSV.

Tratamiento

Solo aquellos casos de WPW que se acompañan de taquidisritmias requieren tratamiento. En niños menores de un año de edad donde es difícil realizar estudios electrofisiológicos invasivos para determinar el mecanismo de la TSV y las características anatómicas y fisiológicas del tracto accesorio se utiliza el *digoxin* en las dósis usuales de acuerdo a la edad y el peso del paciente. Si el paciente ha tenido cambios que sugieran fibrilación atrial debe usarse otro agente antidisrítmico.

El *propranolol* es también efectivo en el control de estas taquicardias. Puede utilizarse en combinación con el digoxin en casos difíciles de convertir.

La combinación de *propranolol y quinidina* ha sido efectiva en los casos de infantes con el síndrome de WPW y TSV repetitiva.

El verapamil es muy efectivo en el tratamiento de la TSV cuando ocurre por reentrada através de un tracto accesorio o a nivel del nodo A-V. El mecanismo debe siempre conocerse antes de comenzar la terapia con este nuevo agente antidisrítmico.

Se he recomendado la *disección quirúrgica* del tracto accesorio cuando:

1) el medicamento no controla la TSV,
2) cuando se demuestra que el tracto accesorio está en la pared libre de los ventrículos y no en el septo interventricular.
3) cuando el paciente es mayor de 3 años de edad.

Actualmente se piensa que el tratamiento quirúrgico es preferible al tratamiento prolongado con múltiples medicamentos.

En los infantes, la tendencia actual es realizar una terapia médica agresiva con la esperanza de que el tracto accesorio cese su funcionamiento con el desarrollo del niño y la consecuente desaparición del WPW y la TSW.

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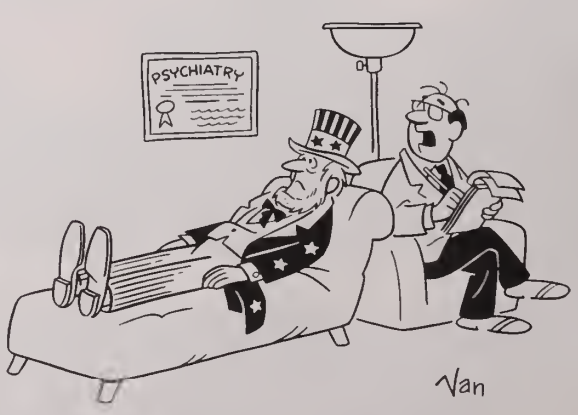

"YOU SHOULD HAVE COME TO ME SOONER."

IMAGENES SONOGRAFICAS Y RADIOGRAFICAS

Rafael Rivera, MD

The patient was a 104 y/o male complaining of epigastric pain, anorexia and weight loss. An abdominal sonogram was requested because the U.G.I.S. done elsewhere revealed no gastric masses. A smooth irregularity along the greater curvature aspect of the stomach was interpreted as suggestive of an extrinsic mass effect (Fig. 1).

The most likely diagnosis is:

A. Hepatic mass
B. Pancreatic tail mass
C. Infiltrating gastric carcinoma (Linitis Plástica)
D. Pancreatic pseudocyst

Correct Diagnosis: C) Linitis Plástica

Discussion

Sonography is an excellent diagnostic modality for detection of hepatic, splenic, pancreatic, renal and biliary abnormalities. The bowel gas, however, prevents sound transmission and precludes proper sonographic evolution of the gastrointestinal tract, Conventional radiographic barium studies are indicated when organic diseases of the bowel are suspected. Sonography, however, can incidentally depict a variety of clinically silent or unsuspected gastrointestinal lesions. These include primary or metastatic carcinomas, indussusceptions, infarctions, hematomas and inflamations[1 2 3 4 5 6 7].

Adenocarcinomas of the gastrointestinal tract produce a focal wall thickening that may surround or grow excentric to the bowel's lumen[1 3 6 8]. The sonographic appearance of the tumor is typical presenting a strong, central luminal echo surrounded by the sonolucent mass. This sign has been reported as highly specific for bowel carcinomas and has been called the "bull's eye", target sign and pseudokidney sign by various authors[1 2 3 4 5 6 7].

Gastric carcinomas are of the polypaid, ulcerative and infiltrating types. Linitis plastica or "leather bottle stomach" is a rare variety of the infiltrating type. The tumor diffusely infiltrates the gastric walls and induces a severe desmoplastic reaction[8]. The stomach becomes rigid and contracted producing the typical radiographic "leather bottle" appearance (Fig. 1). Due to the absence of a focal intraluminal mass the tumor may escape radiographic detection in an early stage as occurred in the presented case. Sonography, however, demonstrated the abnormally thickened gastric walls to better advantage (Fig. 2).

FIGURE 1
Selected view of the patient's U.G.I.S. The stomach presented the same configuration in all the other (not included) films.

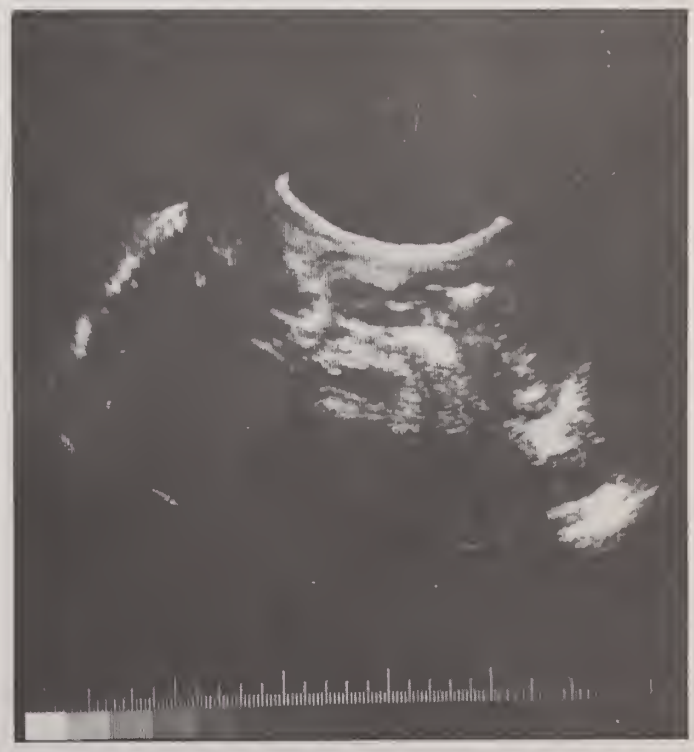

FIGURE 2
Transverse abdominal sonographic section three centimeters below the xyphoid process.

Although sonography is not the ideal diagnostic modality to rule out gastrointestinal tract pathology, the incidental identification of a "bull's eye sign" during an upper abdominal sonogram should raise the possibility of a neoplastic bowel lesion. The patient should be further evaluated by the pertinent radiographic barium studies.

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Fires In Homes Can Be Prevented

Home Fires Kill Many

Next to falls, fires kill the largest number of peole in the home each year.

To prevent the tragedy of a home fire, provide ample ashtrays and don't place them on a flammable table cover. Don't smoke in bed, watch candles carefully and make certain fireplace screens fit snugly.

The American Medical Association points out that the kitchen stove can be a hazardous area. Treat it with caution. Blousy sleeves and frilly aprons invite disaster. Try to keep abreast of information about flammable fabrics.

Keep children and pets away from the stove area while cooking. Store salt and soda near the stove for grease fires. If small children are not secured in high chairs, do not allow them in the kitchen if you have to leave while the stove burners are on.

Be careful with matches around the home. Teach small children early how hazardous fire can be if it is abused.

Regularly and thoroughly clean out attics, basements, closets and stuffed furniture. If you must keep flammable liquids such as gasoline or kerosene, keep them locked up in an outside storage shed.

Electricity is one of the major sources of home fires. Check extension cords for fraying or loose connections and broken insulations, Don't overload wall plugs. Make certain your appliances are in good condition and repair or discard faulty ones promptly. Make electrical repairs yourself only if you are trained to do so. Otherwise, call an electrician.

Learn how to replace a fuse, but find out why it blew. Modern circuit breakers are simple and safe, but it still is necessary to know why the circuit was overloaded.

Make certain your furnace or heating system is clean and in good operating condition. The same applies to water heaters.

October, 1981
Frank Chappell
Science News Editor
AMA

Resumenes de La Literatura Médica

THE SIGNIFICANCE OF GASTRO ESOPHAGEAL REFLUX PATTERNS IN CHILDREN: Jolley, S.G., Johnson, D.G., Herbst, J.J., Matlack, M.E. Journal of Pediatric Surgery. 16:859-865, 1981.

Ninety three consecutive children, less than two yers old were studied, based on a clinical history of gastro esophageal reflux and a confirming 18-24 hr. pH recording test. Refluxing patterns could be classififed in three groups: continuous (type I), discontinuous (type II) and mixed (type III). The type of reflux was an important predictive factor in terms of spontaneous resolution and need for surgical intervention. Type II reflux was most likely to disappear spontaneously (63%) on medical therapy alone. Remission was usually completed by 10 months of age. On the other hand, children with types I and III patterns were significantly less likely to resolve their reflux spontaneously (21% and 13% respectively) and were likely to require surgical intervention (50%). This evaluation may further help in the determination of the management strategies of refluxing infants.

Pedro J. Rossello, M.D.

EFFECTIVENESS OF NISSEN FUNDOPLICATION FOR GASTROESOPHAGEAL REFLUX IN CHILDREN AS MEASURED BY 24-HOUR INTRAESOPHAGEAL pH MONITORING: Berquest, W.E., Fonkalsrud, E.W., Ament, M.E. Journal of Pediatric Surgery 16:872-875, 1981.

Children with severe symptomatic gastro esophageal reflux were evaluated pre and post Nissen fundoplication and compared to children found not to have reflux, using 24 hour intraesophageal pH monitoring and measurement of the lower esophageal sphincter pressure. Nissen fundoplication resulted in a marked reduction in frequency and duration of reflux, to levels below normal controls. This surgical procedure also resulted in an increase in lower esophageal sphincter pressures, but to levels somewhat below normal. Patients were all symptomatically relieved. It is concluded that continuous intraesophageal pH monitoring is a most important test in evaluating candidates for antireflux operations and is a more reliable indicator than lower esophageal sphincter pressures in determining results of therapy. The Nissen fundoplication is effective in controlling gastro esophageal reflux and its complications in children.

Pedro J. Rosselló, M.D.

METRONIDAZOLE: AN ALTERNATIVE THERAPY FOR ANTIBIOTIC-ASSOCIATED COLITIS. Cherry RD, et al. Gastroenterology. 1982;82:849-51.

La vancomicina se considera el antibiótico de elección en pacientes con colitis pseudomembranosa. Se ha reportado que metronizadole también es efectivo en esta condición. Los autores informan de 13 pacientes con diarrea debido a colitis pseudomembranosa asociada al uso de antibióticos y que ellos trataron con metronidazole. la dosis fue de 1.5 a 2 gramos por día por un mínimo de 7 y un máximo de 14 días. Todos respondieron con desaparición de la diarrea en los primeros 5 días. Los autores comentan que la respuesta a metronidazole en estos 13 pacientes fue similar a la esperada con vancomicina y que en su farmacia vancomicina es más de cien veces más caro que metronidazole.

Angel Olazábal, M.D.

RELATIONSHIP BETWEEN PATTERNS OF BLEEDING AND HECOCCULT SENSITIVITY IN PATIENTS WITH COLORECTAL CANCERS OF ADENOMAS. Macrae FA and St. John JB. Gastroenterology 1982; 82: 891-8.

Hace unos años que se determina si muestras de heces fecales contienen sangre usando tarjetas preparadas con guaiac como lo son las tarjetas Hemoccult II. Los autores de este estudio evaluaron la sensitividad de estas tarjetas en detectar sangre en las heces de 72 pacientes con un diagnóstico confirmado de cáncer o adenoma de colon. También estimaron el volumen de sangramiento usando el método de células rojas marcadas con cromio -51. Entre los muchos hallazgos del estudio se encontró que: 1) tumores en el ciego y colon ascendente sangran más (9.3 ml/día vs. 1.8 ml/día para tumores del recto, por ejemplo); 2) la hidratación de la muestra en la tarjeta (se añadió una gota de agua solamente) aumentó significativamente la sensitividad de la prueba (la frecuencia de negativos falsos en pacientes con cáncer bajó

de 31 a 9% ; 3) en los pacientes con adenomas, el volumen de sangre perdido en las heces y la frecuencia en que la prueba de Hemoccult fue positiva para sangre correlacionaron positivamente con el tamaño de la lesión.

Angel Olazábal, M.D.

AGRANDAMIENTO DE LA OREJUELA ATRIAL IZQUIERDA EN LOS ADULTOS: IMPLICACION ETIOLOGICA. Curtis E. Green, M.D., Micael J. Helley, M.D. & Charles B. Higgins, M.D. Radiology 142: 21-27, 1982.

Cincuenta y un pacientes fueron divididos en dos grupos: 20 pacientes conocidos con enfermedad de la válvula mitral de origen reumático y 31 pacientes con agrandamiento del atrio izquierdo de origen no reumático. Este último grupo incluía pacientes con disfunción isquémica de músculo papilar, prolapso de la válvula mitral, y cardiomiopatía congestiva. Estudios radiográficos demostraron que el agrandamiento de la orejuela atrial izquierda estaba presente en 18 de los 20 casos con valvulopatía mitral de origen reumático, pero solo en uno de los 31 con agrandamiento atrial izquierdo de origen no reumático. No se encontró relación directa entre el agrandamiento de la orejuela atrial y el tamaño del atrio izquierdo según establecido por radiografía o por ecocardiografía, o el grado de hipertensión venosa pulmonar, o la presencia de fibrilación atrial. Se postula que la inflamación reumática de la orejuela permite que ésta se dilate fuera de proporción con el cuerpo del atrio izquierdo. En el adulto con hallazgos radiográficos de hipertensión pulmonar venosa, el agrandamiento de la orejuela izquierda es un signo valioso y específico de enfermedad mitral de origen reumático.

Bernardo J. Marqués, M.D.

RELEVANCIA CLINICA DE FOLICULOS LINFOIDES GRANDES EN EL COLON. Phillip J. Kenney, M.D., Robert E. Kochler, M.D. & Gary D. Shackleford, M.D. Radiology 142: 41-46, 1982.

Folículos linfoides grandes fueron demostrados en 17 pacientes mediante el estudio por enema baritada con contraste de aire. Estos variaron en tamaño pero eran al menos de 4 mms. de diámetro y estaban localizados mayormente en la región recto-sigmoidea. Enfermedad inflamatoria intestinal fue encontrada en 13 de estos 17 pacientes (73%) y linfoma en 1. En 100 controles sin síntomas o signos de enfermedad inflamatoria intestinal, los folículos linfoides no excedieron los 3 mm. de diámetro, aunque eran visibles en el 52% de los pacientes menores de 30 años y el 17% de pacientes sobre esa edad. La presencia de folículos linfoides que midan más de 4 mm. en la enema baritada con contraste de aire, se debe considerar enfermedad intestinal inflamatoria o, menos probable, linfoma o disgamoglobulinemia.

Bernardo J. Marqués, M.D.

THE ROLE OF MARROW TRANSPLANTATION IN THE ERRADICATION OF MALIGNANT DISEASE: Thomas Ed. Cancer 1982; 49(10): 1963.

This Kettering award lecture by the recipient of a Research Cancer Award from the National Institute of Allerge and Infectious Diseases, and from the Fred Hutchinson Cancer Research Center in Seattle gives me excellent overview of progress with marrow transplantation.

The two major problems are:
(1) Death from Non Leukemic Causes,
(2) Death from Leukemic Recurrence.

Acute Seattle Marrow Transplant Team is now doing more than 200 transplants/year.

Marrow transplantation is an accepted form of therapy for several types of human disease.

We recommend this article for all hematologists interest in leukemia research.

Arturo Ydrach, M.D.

NATIONAL CANCER INSTITUTE SPONSORED STUDY OF CLASSIFICATIONS OF NON-HODKIN'S LYMPHOMA CANCER 1982; 49(10):2112.

This is a unique multiinstitutional study of 1175 cases of Non-Hodkin's Lymphoma sponsored by the National Cancer Institute.

There are at least six well described histopathologic system for Non-Hodkin's Disease. All six classifications were formed to be valuable and comparable in reproducibility and clinical correlations. A working formulation is described which separates the disease into ten major types.

This working formulation was not devised to supplant any currently utilized classfications. The formulation provides a means of transplanting terminology for comparison of trials.

It is obvious that in this very controversial area of the pathological classification of Non-Hodkin's Lymphona this working formulation will be very helpful in comparing results from various investigators.

Arturo Ydrach, M.D.

PELIGROS DE LA RESISTENCIA A TRIMOTHOPRIM-SULFAMETHOXAZOLE.

Trimethoprim-sulfamethoxazole (TMP-SMX) está siendo utilizada con frecuencia como profilaxis para sepsis gramnegativa en pacientes con granulocitopenia. TMP-SMX, junto con nistatin oral o amfotericina B, inhiben el crecimiento de bacterias gastrointestinales patógenas y no tienen efecto en bacterias anaeróbicas endógenas, las cuales inhiben

el sobrecrecimiento de otros organismos.

Wilson y Guiney describen el caso de dos pacientes con leucemia aguda y granulocitopenia que desarrollaron sepsia con Enterobacteriaceae resistente a TMP-SMX. Del cultivo de sangre de uno de ellos, después de 8 días de tratamiento con antibiótico, se aislaron *Klebsiella penumoniae* y *Escherichia coli*. Del otro paciente solo se aisló. *E. Coli* después de tramiento. Ambos pacientse murieron de sepsis incontrolada.

En dos casos la resistencia de estos organismos a TMP-SMX se demostró podía ser transferida por plásmidos, y en un caso se pudo asociar la resistencia con el DNA de la bacteria. Los plásmidos responsables d ela resistencia a TMP-SMX también inducían resistencia a ampicilina y carbenicilina. La evidencia indica que esta resistencia puede ser transferida in vivo. (Wilson, J.M., y Guiney, D.G.: N. engl. J. Med. 306:16, 1982).

Comentario: Además de la evidencia presentada aquí, se han realizado otros estudios en Europa que revelan el surgimiento de una Enterobacteriaceae con un plásmido con resistencia a TMP-SMX. Debido al aumento en el uso de TMP-SMX como profilaxis, esta resistencia puede resultar un problema serio; añadiendo a ésto el plásmido con resistencia a carbenicilina, otro antibiótico utilizado rutinariamente para sepsis en pacientes con granulocitopenia.

C.H. Ramirez-Ronda, M.D.

EVALUACION MUSCULAR MULTITERRITORIAL PARA CONTRACCIONES ISOMETRICAS MAXIMAS DEL MUSCULO DELTOIDE EN HUMANOS NORMALES Y DISTROFICOS. Simard T Vorro J and Rocque P. Am J. Phys Med. 60:132-143, 1981.

El uso de potenciales de EMG puros con electrodos de alambres cuadribipolares, junto con potenciales rectificados y filtrados permitió la cuantificación de diferencias con la actividad territorial indivudal en el músculo deltoide de sujetos normales y distróficos durante contracción isométrica máxima. Los resultados indican que en distrofia muscular tardía los pacientes mostraban patrones de interferencia de niveles bajos a través de la contracción.

Manuel Naredo, M.D.

MECANISMOS DE LA TAQUICARDIA CON INTERVALO QRS AMPLIO EN NIÑOS: Benson SW, Smith WM, Dunnigan A, et al. Am J Cardiol, 1982; 49: 1778.

Se informan los resultados de los estudios electrofisiológicos invasivos en 32 pacientes con taquicardia de QRS amplio cuyas edades fluctuaron entre 1 mes y 18 años.

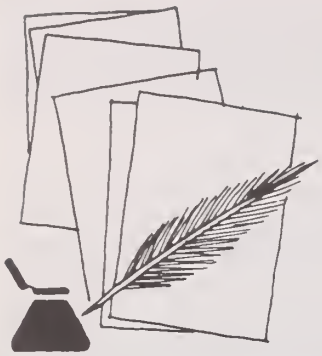
Se demostraron 5 mecanismos básicos en este tipo de taquicardia:

1) Taquicardia reciprocante ortodrómica con bloqueo de rama. En ella hay una activación ventricular através del sistema de conducción normal con activación atrial retrógrada através de un tracto A-V accesorio. Este tipo se demostró en 7 casos.
2) Taquicardia reciprocante antidrómica —En este tipo la dirección de la conducción se invierte: la conducción A-V ocurre por una vía accesoria y la conducción VA lo hace por el sistema de conducción normal, (3 casos) o por un tracto accesorio adicional. (Kent, 3 casos)
3) Aleteo atrial con preexcitación ventricular através de tractos accesorios. En estos casos los tractos accesorios no son esenciales para el mecanismo de la taquicardia. (8 pacientes)
4) Taquicardia reciprocante através de un tracto accesorio nodoventricular (Mahaim) — 5 pacientes. En este mecanismo el tracto accesorio es la vía anterograda del macrocircuito de reentrada con el haz de His-Purkinje y parte del nodo A-V como la vía retrógrada.
5) Taquicardia ventricular —Fue en general un diagnóstico de exclusión. Se diagnosticó en 6 pacientes, se utilizaron los siguientes criterios diagnósticos.
   a) los mecanismos 1, 2, y 3 estaban ausentes
   b) tractos accesorios ausentes
   c) los atrios no participaron en la taquicardia

El estudio demuestra que las taquicardias con QRS ancho no son raras en los niños. Su mecanismo es complejo y el análisis electrocardiográfico con respecto a la configuración del QRS, la frecuencia cardíaca, y la presencia o ausencia de disociación atrio-ventricular no es suficiente para el diagnóstico.

Los resultados revelan que es difícil distinguir los mecanismos de este tipo de taquicardia aunque éstos pueden entenderse mejor mediante la evaluación de la conducción A-V y V-A con las técnicas de electroestimulación. Es esencial el conocer estos mecanismos para poder determinar la actitud terapéutica indicada, ya bien sea mediante el uso de medicamentos, de procedimientos quirúrgicos, o implantación de marcapasos.

Rafael Villavicencio, M.D.



CARTAS AL EDITOR

Tomografía Computarizada del Cerebro... ¿Una Panacea?

En el primer artículo del Boletín de la Asociación Médica de Puerto Rico correspondiente al mes de febrero de 1982 con relación al diagnósticos de metastasis cerebrales utilizando la Tomografía Computarizada (CT), los autores resumen que el "CT no es la panacea en la detección de metastasis en el cerebro". La Tomografía Computarizada (CT) en este momento histórico de la medicina puertorriqueña, si no es la panacea para la investigación de enfermedades cerebrales está bien cerca de serlo, particularmente en la neurocirugía traumatológica. La utilización de esta modalidad de diagnóstico ha cambiado radicalmente la práctica de las ciencias neurológicas y en particular el manejo del paciente con traumatismo a la cabeza.

Nuestra experiencia en el Departamento de neurocirugía del Centro Médico de Puerto Rico (CMPR) durante los últimos 12 meses atestigua al cambio radical en el manejo agudo y seguimiento de los pacientes traumatizados. Previo al establecimiento del CT en el CMPR, estos pacientes eran sometidos a arteriografía cerebral y descompresión de hematomas extracerebrales utilizando parámetros crudos de localización anatómica y muchas veces por razón de cambio brusco en el cuadro clínico del paciente. Muchas veces las radiografías simples de cráneo y arteriografía no añadían más información que la que el neurocirujano podía obtener mediante un examen neurológico y fondo de ojo.

El diagnóstico de hemorragia sub-aracnoidea, intra ventricular e intra cerebral no podía establecerse con métodos radiológicos directos y menos aún el diagnóstico de contusión, edema cerebral e hidrocefalia aguda post-traumática. Todas esas entidades patológicas se describían en la sala de operaciones o en la sala de autopsia. El uso del CT como método de diagnóstico primario en todos los casos de trauma a la cabeza es indiscutible.

En estos momentos de gran preocupación por los altos costos de los servicios médicos, es necesario que cada médico evalúe cuidadosamente a su paciente para decidir los procedimientos y en qué orden se deben hacer para establecer un diagnóstico. En otras palabras, un buen examen físico no debe ser suplantado por un procedimiento de diagnóstico, cualquiera que sea. ¿Cuáles son las indicaciones para ordenar un CT de cabeza? Cualquier condición clínica que le sugiera al médico la posibilidad de una lesión intracerebral. Esto presupone un exámen neurológico.

¿Cuáles son las contraindicaciones? El CT de cabeza sin contraste no tiene ninguna contraindicación. El CT con contraste tiene las mismas contraindicaciones que cualquier estudio radiológico que requiera la inyección de contraste yodado.

¿Es el CT un estudio primario o secundario? En aquellas situaciones clínicas donde se sospecha patología intracerebral el CT es el arma de diagnóstico primario. De hecho los hallazgos de CT orientarán el manejo de la condición clínica del paciente.

¿A cuánta radiación se expone el paciente en un CT promedio? Un CT de cabeza expone al paciente a una dosis de radiación similar a la de una serie de cráneo ("Skull Series").

¿Cómo se ha influenciado el manejo de trastornos cerebrovasculares? Antes del CT era prácticamente imposible diagnosticar infartos cerebrales y menos aún la extensión de la lesión. El CT diferencia entre infartos isquémicos y hemorrágicos, haciendo posible que el médico pueda instituir el tratamiento apropiado de acuerdo al tipo de infarto.

¿Cómo se ha influenciado el manejo del paciente con un tumor cerebral? El CT le muestra al neurocirujano la extensión anatómica del tumor, sus características, le provee información sobre la necesidad de arteriografía selectiva y ayuda en la planificación de la operación. Se ha eliminado casi totalmente la arteriografía cerebral y el escintigrama en el manejo post operatorio del paciente.

Aunque en el CT todavía hay algunas dificultades en la evaluación de la fosa posterior, en este momento es el mejor instrumento de diagnóstico para lesiones intracerebrales.

La Tomografía Computarizada de la cabeza es un procedimiento de diagnóstico de la radiología y su interpretación recae sobre aquellos que han sido adiestrados en la interpretación radiológica.

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U. S. ARMY MEDICAL DEPARTMENT

First Year Graduate Medical Education

General

The Army Medical Department (AMEDD) operates the largest unified Graduate Medical Education (GME) program in the United States and probably in the free world. The AMEDD is one of the most mature educational systems in America. The AMEDD's purpose is to conduct quality GME in accredited programs of the specialties and numbers needed to produce a Medical Corps composition and strength that is appropriate to the needs of the total Army. Programs are conducted at all eight medical centers and at five community hospitals (Forts Benning, Belvoir, Bragg, Hood and Ord), but through outreach programs from these parent facilities many other Army hospitals are involved with residency training. All Army medical training programs are approved by the Council on Medical Education of the American Medical Association. Virtually all recognized residencies are offered. Each Army training hospital is affiliated with a leading nearby medical school. The range of cases, both in complexity and age, is virtually impossible to duplicate and medical records keeping is excellent. The well trained and competent ancillary support staff of an Army Hospital allows residents to spend a majority of their time treating patients, not doing chores. Also, we have designed our programs to ensure that our residents are used as full-time doctors—not part-time, tag-along onlookers. Total patient care responsibility is stressed.

Application

During the summer of 1983 the AMEDD will offer approximately 350 First Year Graduate Medical Education (FYGME) positions. Historically, most positions are filled by medical school graduates who were Army scholarship participants. However, the AMEDD actively seeks highly qualified civilian student applicants who have no current affiliations. FYGME programs are available in the flexible, categorical and categorical diversified categories.

Deadline for applications is 1 September 1982. All applicants are encouraged to also participate in the NIRMP. Selections for the Army FYGME Program will be announced in sufficient time for selectees to withdraw from the NIRMP.

To find out more information concerning this program, the eligibility criteria, service obligation, benefits, and application procedures contact:

AMA NEWS

A SINGLE DOSE CURE FOR CYSTITIS

About 20 percent of women have a urinary tract infection called cystitis at least once in their lifetimes. For many years, treatment has usually involved taking prescribed drugs for seven to ten days to kill the bacteria that cause the disease.

This conventional therapy may increasingly be replaced, however, by treatment with single doses of drugs containing sulfisoxazole alone or a combination of triemthoprim and sulfamethoxazole.

Researchers from the University of Manitoba, Canada, report on results of their own and other studies testing the single-dose treatment for cystitis. In the Canadian study, headed by Frederick J. Buchwold, MD, the overall rate of cure in women with urinary tract infection confined to the bladder treated with various sized single doses of medication was 95 percent. However, Buchwold, who is now in practice in San Antonio, Texas, and his colleagues report a lower rate of cure —69 percent— in their patients with signs of kidney involvement.

Other studies cited by the authors found that several different drugs in single doses are suitable for treating acute, uncomplicated urinary tract infections localized in the bladder.

An accompanying JAMA editorial by Steven A. Lerner, MD, and Thomas Fekete, MD, of the University of Chicago School of Medicine, states: "There is no question that single-dose therapy for lower urinary tract infection can be safe and effective." But, they add "some unanswered question remain."

Studies no far have involved relatively small numbers of nonpregnant women only. Lerner and Fekete suggest future studies should involve larger numbers of patients and should also include pregnant women. In pregnant women, they note that single dose therapy, if effective, would have the usual advantages of lower cost and fewer side effects and, in addition, would decrease the drug exposure of their unborn children.

Future studies also should include men and groups of patients with more complicated cystitis including kidney involvement, according to the editorial.

LONG TERM SAFETY OF ULTRASOUND ON FETUS STILL UNRESOLVED

In the past ten years, ultrasond has developed from a research instrument into a valuable and widely used diagnostic tool, allowing obstetricians to "see" inside the womb. But at a symposium concerning the effects of ultrasound on the fetus, researchers and clinicians shied away from recommending the routine use of ultrasound in prenatal care, citing their inability to quantify its risk.

Until physicians can say with assurance that ultrasound does not produce subtle or delayed harmful effects, it should be used only when medically indicated, most of the participants agreed.

The concern over the potential harmful effects of ultrasound is based on the results of animal and other laboratory studies in which abnormalities have been produced. For the most part, however, these abnormalities, which range from weight reduction in mouse or rat fetuses to damage in insect eggs, cannot yet be extrapolated to humans.

Ultrasound is known to produce biological effects in cells and in laboratory animals by at least two mechanisms —heat and a process called cavitation, in which air bubbles expand and contract in response to sound waves, according to the report in the JAMA.

Despite the lack of an unqualified go-ahead for routine prenatal ultrasound testing, there apparently are not even anecdotal reports of harmful effects in children exposed to ultrasound before birth. Preliminary results from a large study in progress in Canada, reported at the meeting sponsored by Columbia University College of Physicians and Surgeons and the March of Dimes Birth Defects Foundation in New York, are similarly reassuring.

The study, begun five years ago at the University of Manitoba, Winnipeg, includes 10,000 women and their offspring who were exposed to diagnostic ultrasound *in utero*. According to Edward A. Lyons, MD, director of ultrasound at the university's Health Science Center, preliminary analysis of available data indicate nothing unusual in the exposed children.

Because it is now possible with ultrasound technology to perform a physicial exam of the fetus in th womb, as Harold E. Fox, MD, of Columbia University said, the question in many obstetricians's minds is whether all pregnant women should be screened with diagnostic ultrasound.

Fox estimated that about half of all pregnant women receiving care in an institutional setting are examined by diagnostic ultrasound. Far fewer women, however, recieve such examination in the offices of their private obstetricians, according to preliminary results of a survey by the American College of obstetricians and Gynecologist (ACOG). Only 30 percent of the patients of private practitioners in the ACOG survey received one ultrasound scan, and only 20 percent were scanned more often.

Among the respondents —about 12 percent of ACOG's 23,000 members— only 15 to 20 percent owned office scanners, and of those, only 10 percent said they scanned all of their patients.

While scientists grapple with ultrasound's unknowns, how should obstetricians respond? Prudently, the symposium panelists said. That translates as advice to use ultrasound when necessary, as in the evaluation of high-risk pregnancies, but not routinely for all pregnancies.

INFANT WALKERS CAN BE HAZARDOUS TWO PHYSICIANS SAY

Special seats for children riding in automobiles and toxic substances left where children can get hold of them have been

well publicized in articles directed at safeguarding the welfare of children. Now comes another hazard for youngsters: the infant walker.

According to two pediatricians writing in the *American Journal of Diseases of Children,* not only is there no proven benefit from the use of walkers, but also these seats on wheels can actually be dangerous.

In their survey of parents of 150 children between the ages of five and fifteen months —all users of infant walkers— Carol A. Kavanagh, MD, and Leonard Banco, MD, found that 47 children suffered mishaps in their walkers. Most had bruises and abrasions, but some had serious head injuries when the walkers either tipped over or fell down stairs.

Kavanagh, who is with the Joseph C. Wilson Health Center in Rochester, N.Y., and Banco, who is with Hartford Hospital in Connecticut, admit that their study lacked a control group who did not use walkers for comparison. Nevertheless they conclude in their report that infant walkers are associated with a significant risk of injury, at least with their present design.

Infants, they said, certainly learn to walk without the practice they get in an infant walker; and they cite a study done elsewhere which found that infants who did not use walkers were walking slightly earlier than their siblings.

MORTALITY OF JOGGERS

Dr. Paul Thompson and his colleagues report that during a six-year period only 12 men died during jogging in Rhode Island. The authors then estimated how many joggers were active in this period, using a random telephone survey, and concluded that one death occurred per year for every 7,620 joggers, or per 396,000 man-hours of jogging.

All but one of these deaths were presumed to have been due to coronary heart disease (CHD). Coroners autopsies disclosed one or two-vessel CHD in six cases. The coroner elected not to permorm autopsies in three other cases in which there had been a clinical history of CHD. Almost half of the deaths (five) occurred in men in whom a premortem diagnosis was possible; however, even discounting these deaths, death occurred more often during jogging than would be expected by chance. The meaning of this is not certain, because it is not clear what proportion of joggers had known heart disease and were pursuing this form of exercise for rehabilitative purposes. However, they were not novices, for in all but one of the deaths (eight) where a running history was available, the runner had been jogging regularly for a year or longer.

Even though much of the data we would like to have is missing, these data are the most inclusive that are available on this subject to date. Because mortality during jogging is so low, it is suggested that pretesting with a submaximal exercise test is not warranted. However, doubts remain, because there are no data on how many joggers may have precipitated nonterminal symptoms during jogging that would have permitted them to find medical attention, and perhaps even resulted in hospital admission before death, precluding a coroner's investigation. Furthrmore, there are no good data on the characteristics of the population involved, ie, the burden of CHD risk factors, the overall age, incidence of known CHD, and the intensity of exercise in the jogging population.

It is interesting that no mention is made of automobile accidents, attack by vicious dogs, traumatic injuries, or other misadventures that may befall joggers. Because of the increasing popularity of jogging, the Insurance Institute of Highway Safety made a study of 60 jogger-motor vehicle collisions for the year 1978-1979 that were identified by newspaper accounts and police reports in 28 states. Thirty of the joggers were killed. More than half of the collisions occurred after dark. The fault was assigned to the jogger about as often as to the driver. Thus, this may be an important jogging hazard in some urban communities, although the prevalence of jogging in these 28 states is not known.

Jogging has become such a popular sport, and its practitioners, including many physicians, are so convinced of its benefits for both cardiac patients and for the well population that the importance of obtaining further data on medical complications in men and women, with and without known coronary disease, cannot be debated. A new effort is planned to this end by the American Medical Joggers Association. The 4,000 members of this organization have responded to a rather elaborate questionnaire detailing their knowledge of their own demographic caracteristics, medical history, CHD risk factors, running behavior, and possible modification of risk factors by running. They will be compared with a larger sample of randomly selected physicians surveyed in similar fashion. This small study will not supply morbidity and mortality data of any significance immediately, but it should provide a better profile of physician-joggers and the incidences of CHD and risk factors in this group, as compared with nonjogging physicians. If this population can be followed up for a few years, perhaps morbidity and mortality data will be obtained.

FIRST IMPLANTATION OF REMOTE CONTROLLED INSULIN PUMP REPORTED

A remotely programmable insulin pump has been successfully implanted for the first time in an insulin-dependent diabetic man, according to a report in the *Journal of the American Medical Association.* The device has been functioning well for over a year.

Physicians from the University of New Mexico School of Medicine in Albuquerque, led by endocrinologist David S. Schade, MD, Associate Professor of Medicine, implanted the pump in January 1981 in a then 41-year old man who has had diabetes since the age of five years.

With use of the implanted pump, the patient's blood sugar levels (which fluctuate with food intake and exercise) were controlled better than they were when he was giving himself daily injections of insulin during a pre-implant evaluation.

The insulin pump consists of a silicone rubber insulin reservoir (implanted in the abdomen just below the skin so that it can be refilled by injection) and the sealed pump itself, which is controlled by a palm-size, push button unit permitting the recipient to program and measure the rate and quantity of insulin delivered by the pump. The insulin is continuously pumped into the abdomen and absorbed into the bloodstream by capillaries.

In an editorial accompanying Schade's report, three Mayo Clinic endrocrinologists —F. John Service, MD, Robert A. Rizza, MD, and John E. Gerich, MD,— emphasize the experimental nature of insulin infusion devices. The benefit of an implanted pump over one which is worn on the outside of the body, they say, may be largely cosmetic. The risks, which include reservoir leakage and pump malfunction, have yet to be fully assessed.

HEPATITIS B VACCINE MAY INDIRECTLY PROTECT AGAINST LIVER CANCER

As evidence linking hepatitis B virus to liver cancer continues to mount, the use of the newly licensed vaccine against the virus is being seen as a possible way to protect against this single form of cancer, according to an editorial by Harvey J. Alter, MD, in the *Journal of the American Medical Association.*

Alter, who is chief of the immunology section at the National Institutes of Health Clinical Center Blood Bank Department, foresees the possibility that hepatitis B vaccine may become, at least indirectly, the first cancer vaccine by conferring protection against the hepatitis B virus, thereby breaking the chain of events that is thought to lead to liver cancer in some people.

Hepatitis B vaccine, which is due later this year, is expected to decrease the incidence of hepatitis B infection and reduce the number of hepatitis B carriers, who are at high risk for developing liver cancer.

There are approximately 800,000 hepatitis B carriers in the United States, Alter said, and they are not only at risk for developing life-threatening liver disease, including cirrhosis and hepatocellular carcinoma, but they also pose a serious threat to the health of their families and sexual partners.

Hepatitis B virus, which is composed of a core particle of genetic material and a surrounding coat of protein, is transmitted through conact with infected blood or blood products and through contact with other infected material, including secretions such as saliva and semen. The virus can enter the body through a burn, scratch, cut or puncture —any break in the skin. During the acute stage of infection, coat particles are produced in far greater numbers than are the complete viruses because of defect in viral reproduction. The hepatitis B carrier state is characterized by the presence of coat particles —otherwise known as hepatitis B surface antigen in the circulation.

The hepatitis B vaccine is made of hepatitis B surface antigen obtained from the blood of carriers. Targets for the vaccine will be people whose jobs, living condicitons, sexual practices and medical status put them at high risk for exposure to the disease. As enumerated by Alter, these include:

- health workers having direct patient contact, particularly those expose to patient's blood and blood products.
- renal dialysis patients;
- institutionalized patients and their attending staff, particularly in facilities for the mentally retarded;
- patients with medical disorders requiring repeated blood transfusions;
- male homosexuals;
- sexual partners and household contacts of hepatitis B carriers;
- newborns whose mothers are hepatitis B carriers;
- children and susceptible adults in locals where hepatitis B is endemic.

It is estimated that there are 200 million hepatitis B carriers worldwide, with a high incidence in Africa, Southeast Asia and parts of South America. "The greatest potential use of the vaccine is in the developing nations of the Third World", Alter says. But the vaccine's high cost, a consequence of the long and complicated manufacturing process, could make it inaccessible to the populations that need it most, he warns.

Alternate methods for developing hepatitis B vaccines are being considered, including production of synthetic antigen and production of antigen by bacterial cells engineered using gene-splicing techniques.

Other approaches to eradicating the hepatitis B carrier state are also under investigation. Another report in the current JAMA presents findings of a small-scale human trial at Stanford Univeristy School of Medicine to eradicate the viral infection using a combination of vidarabine monophosphate, which inhibitis viral reproduction, and human interferon. A larger double-blind trial to evaluate this regimen is being carried out by the Stanford research team, which includes Thomas C. Merigan, MD, head of the school's Department of Infectious Diseases and one of the nation's foremost investigators of interferon.

JAMA CONTEMPO ISSUE

In a departure from our regular news releases, I want to draw your attention to a special issue of the *Journal of the American Medical Association* called *Contempo 1982* in which the editors draw together authors from diverse specialties in medicine to report on the latest clinical accomplishments in their fields.

This special JAMA, is the fifth in the annual Contempo series. If a common thread linking many of the significant articles in this issue can be found it is human reproduction.

Authors of articles on "Urology," "Obstetrics and Gynecology" and "Surgery" highlight the details of *in vitro* fertilization and review the progress in pioneering *in utero* surgery. A companion article on "Biomedical Ethics" by the director of the Center for Bioethics of the Kennedy Institue explores the special concerns about the fetus that have arisen in such sharp relief this year.

Authors on "Oncology", "Sports Medicine" and "Hematology" look at athletes' amenorrhea, impotence, and the special reproductive concerns of persons with hemophilia —people who not too long ago rarely attained childbearing age.

Other articles delve into the role of genetics in depression, touch on the use of monoclonal antibodies in the treatment of graft rejection, and examine new wrinkles in infectious disease from chlamydial VD (arguably the most prevalent form of sexually transmitted disease) to the recent evidence concerning herpes virus and cervical cancer.

We have reserved a number of copies of the special *Contempo* issue and will be happy to accommodate your needs to the extent of our supply.

A table of contents follows, and for those of you interested in only one or two articles, we will duplicate copies and get them to you as quickly as possible should you want to prepare stories prior to the day-of-issue embargo date.

IMPAIRED PHYSICIAN CONFERENCE SET FOR SEPTEMBER

The American Medical Association will hold its Fifth National Conference on the Impaired Physician in Portland, Oregon, September 22-25, 1982. The meeting is sponsored jointly by the Oregon Medical Association and the AMA and will be held in the Portland Marriott.

Physician impairment, whether due to drug abuse, alcoholism, mental illness or senility, has long been of concern to the AMA. For the past ten years, the Association has actively encouraged all segments of the medical community to recognize and treat the problems of the impaired physician and, periodically, hosts national meetings to bring together experts in the field.

The theme of this conference is "1972-1992: A Decade of Progress - A Decade of Promise", and topics include: the physician's health in a changing society, preventing burnout, stress and the practicing physician, and a discussion on medicine's responsibility for impaired physicians and other professionals. The conference program has topics of concern to medical students and physicians at various experience levels-residents, practicing physicians and elderly physicians.

A progress report on the Physician Mortality Project, a cooperative venture of the AMA and the American Psychiatric Association, will also be presented.

EDUCACION MEDICA CONTINUADA

ASOCIACION LATINOAMERICANA DE DIABETES
V CONGRESO LATINOAMERICANO DE DIABETES

4 a 8 Abril de 1983, Santiago, Chile
Secretaría General, Chacabuco 419, 2do. Piso, Santiago, Chile

La Asociación Latinoamericana de Diabetes eligió a la ciudad de Santiago de Chile como sede del V Congreso Latinoamericano de Diabetes, evento a desarrollarse entre el 4 y 8 de Abril de 1983.

El Comité Directivo del Congreso al tomar esta responsabilidad, se fijó como objetivo organizar un torneo que logre no sólo excelencia científica, sino que sea motivo de unión y amistad entre todos los profesionales médicos y de colaboración médica que trabajan en Latinoamérica en el campo de la diabetes.

Con este doble espíritu invitan a concurrir a la cita de Santiago de Chile, a fin de alcanzar el éxito que la diabetología latinoamericana se merece. El brillo del V Congreso Latinoamericano no dependerá de este Comité Directivo, que es sólo un intermediario, sino del apoyo generoso que Uds. le brinden con su asistencia.

AMERICAN ACADEMY OF DERMATOLOGY

X PEDIATRIC DERMATOLOGY SEMINAR

The 10th Pediatric Dermatology Seminar will convene at the new Carillon Beach Hotel, Miami Beach, Florida, February 24-27, 1983. Guest Speakers will include: Yehudi Felman, Arthur Norins, Heinz Eichenwald, Arthur Rhodes, Guinter Kahn, Mark Dahl, Lawrence Schachner, etc. The seminar fee is $240.

A seventeen day post-seminar tour to China will visit Kweilin, Hangchow, Peking, Wuxi, Shangai, Suzhou, and Hong Kong. (All inclusive costs, $2395) CME credit is given.

For information contact: Guinter Kahn, M.D., 16800 N.W. 2 Ave. No. 401, Miami, Florida, 33168.

CENTRAL DIVISION CONTINUING EDUCATION

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AMERICAN ACADEMY OF PEDIATRICS

PEDIATRICIANS ADVISE AGAINST ASPIRIN FOR FLU AND CHICKEN POX

Members of a Committee on Infectious Diseases of the American Academy of Pediatrics have reviewed epidemiologic studies of the rare childhood disease Reye Syndrome and concluded it is problable that salicylates, such as aspirin, contribute to the disease. The Committee advised that aspirin should not usually be given to children with suspected cases of chicken pox or influenza.

The Committee, in fact, questioned whether any fever control medications should be given when symptoms of either chicken pox or influenza arise. When physicians believe a fever must be controlled, alternatives such as increased fluid intake and tepid water sponging should be used, said the Committee.

The Committee is chaired by Vincent A. Fulginiti, M.D., chairman of the Department of Pediatrics at the University of Arizona Medical School.

The recommendation follows a similar one issued in February by the government's Centers for Disease Control. CDC's advisory to physicians and parents was based on an expert panel's review of three studies. Several of the panel members are also members of the Academy which alerted its member pediatricians to the panel's concerns at that time through the organization's newsletter.

However, the AAP has suggested to the National Academy of Sciences, a private research organization, that a review of the aspirin-Reye Syndrome association be conducted because portions of the scientific community question the data from the studies.

Critics have claimed there are flaws in the methodology used in the studies, which were conducted in Arizona, Michigan and Ohio. The studies, all but one unpublished, indicated a statistical —but not necessarily a cause and effect— relationship between the use of aspirin for children's viral infections and Reye Syndrome.

Both the CDC panel and the AAP committee conceded that their recommendation was made without absolute proof of casualty but said the present evidence of aspirin association with Reye Syndrome is too strong to be ignored.

The Committee said parents should not administer salicylates for suspected chicken pox and influenza and it went further in calling for "a total community effort". "We urge that governmental agencies undertake appropriate review and necessary action to inform the public at large. We also believe that manufacturers of salicylates should cooperate in informing prospective users of the relationships detailed in this report. Physicians and pharmacists can contribute to this total effort by individual counseling of parents regarding the potential hazards of salicylate use in influenza and varicella (chicken pox). The inclusion of salicylates in many common over-the-counter remedies should encourage parents to scrutinize the labels of all products to be administered to their children."

CDC estimates that 600 to 1,200 cases of Reye Syndrome occur each year in the U.S., mostly in children between the ages of 5 and 14, and that death results in 20-30 percent of the cases and permanent brain damage in many others. The disease first appears as a viral illness (such as flu or chicken pox) with a sudden onset of fever, vomiting and headaches, but progresses rapidly to convulsions and coma.

PEDIATRICIANS ISSUE NEW REPORT ON INFECTIOUS DISEASES

The 19th edition of *The Report of the Committee on Infectious Diseases,* a reference manual widely used by pediatricians and other professionals who provide medical care for children, has been published by the American Academy of Pediatrics (AAP) and is now available for purchase.

Commonly called "the Red Book", the manual provides guide lines for effectively controlling children's infectious diseases. The *Report* first was published in 1938, and is revised by the AAP's Committee on Infectious Diseases every few years to include current, "state of the art" information. Intended for pediatricians and other medical professionals, the Red Book also is of interest to public health officials, hospital personnel and others active in children's health care.

The latest edition includes information on new vaccines and specific immune globulin preparations for hepatitis B, rabies, chicken pox, and pneumococcal infections. Other new sections cover Kawasaki disease, information sheets for parents about immunizations, and tables showing agents which cause common childhood diseases.

The Red Book is available for purchase for $15.00.

AMERICAN COLLEGE OF PHYSICIANS

GENETIC ENGINEERING HAS POTENTIAL TO ABOLISH SOME METABOLIC DEFECTS

Recombinant DNA technology is opening new ways to study cellular regulation and may provide innovative approaches to medical therapy, John D. Baxter, M.D., and investigator at the Howard Hughes Medical Institute told physicians during the recent annual scientific meeting of the American College of Physicians (ACP).

One of genetic engineering's most exciting potential applications, according to Dr. Baxter, is transferring genes initially isolated with the use of bacteria back into mammalian cells. By transplanting human genes into human

cells, he said, medical treatment would not aim at compensating for a metabolic defect —it would actually work to abolish the defect.

To illustrate, Dr. Baxter said pancreatic islet cells could be obtained from the patient by biopsy, grafted with normal insulin genes, and reinjected into the pancreas, where they would presumably thrive and secrete insulin.

"Such a development will require much more knowledge of genes and gene regulation than we now posses," he stressed. "But it seems safe to say that this knowledge will come —not least because of the recent advances in recombinant DNA research."

Applications of bacterial protein synthesis which can be expected in the near future, Dr. Baxter indicated, include production of pure antigens that would facilitate the production of save vaccines; pure antibody to treat infections that do not respond to chemotherapy; pure factor VIII to treat hemophiliacs; and interferon to treat viral infections and cancer, perhaps.

"Another possible medical application of recombinant DNA techniques concerns the prenatal diagnosis of genetic disease," Dr. Baxter commented. "A quicker method than the one currently used is to test not the metabolic products of the genes but the genes themselves by hubridizing the cellular DNA against a standard DNA probe."

Within a few years, he suggested, pure human insulin produced in bacteria will be available at a price competitive with animal insulin. Human growth hormone, currently used to treat some forms of pituitary dwarfism, is being produced in similar ways, he pointed out.

RECOMBINANT DNA TECHNIQUES REVEAL NEW FACTS ABOUT HEPATITIS B VIRUS

"Being able to clone and determine the DNA sequence of the hepatitis virus has revolutionized our ideas of the virus itself," William J. Rutter, MD, told physicians attending the American College of Physician's (ACP) recent scientific meeting.

"The hepatitis B virus was previously thought to be more complicated than it actually is," Dr. Rutter, the chairman of the University of California, San Francisco's Department of Biochemistry and Biophysics, said.

"Hepatitis B has been one of the scourges of mankind for centuries," he stated. About 200,000 new cases of hepatitis B are documented in the United States each year, in Africa, Southeast Asia, parts of South America and southern Europe, the disease is endemic.

"Until recently," Dr. Rutter said, "the hepatitis B virus and the disease itself have been difficult to study. The virus hasn't been cultivatable in tissue cultures and a good animal model for the hepatitis virus hadn't been found."

By using recombinant DNA techniques, however, his laboratory has gained insight into the structure of the virus and how the virus replicates. These techniques also allow the researchers to clone the virus and precisely determine its DNA sequence, Dr. Rutter said.

Although exactly how the virus causes liver disease is still being studied, scientists are now able to produce a particle which could be the basis for a vaccine against hepatitis B, he said.

Dr. Rutter also has used recombinant DNA techniques to develop a system for the expression of the surface antigen gene in both bacteria and yeast.

"In the yeast system," he explained, "surface antigen combines with membrane components of yeast to form a particle similar to those found in the sera of hepatitis B-infected patients." This is the first time recombinant DNA techniques have been used to result in a host cell producing a particulate structure, he pointed out. Usually, recombinant DNA techniques are used to amplify DNA, perhaps make RNA, and —very rarely— produce actual proteins. This technique has the potential to produce far more doses of vaccine than the current production method, which derive vaccine from surface antigen in the blood of human carriers.

Inflammation of the liver is not the sole consequence of hepatitis B infection, Dr. Rutter emphasized. "There is now persuasive evidence that hepatitis B virus is a major cause of hepatomas —the most prevalent form of cancer."

Evidence from other investigators, Dr. Rutter said, indicates that hepatitis B carrier patients are at about 400 times greater risk for primary hepatocellular carcinoma than normal persons —or even patients with hepatitis.

"Our studies", he continued, "suggest that transformation may be associated with integration of the virus in the host genome." His research also indicates that integration occurs at certain preferred sites in the host cell DNA, he said.

"Many carrier patients also have integrated hepatitis B viral sequences in their DNA," he observed, "whereas hepatitis patients are much less likely to have integrated DNA. This correlation strongly indicates the probable causality of hepatitis B virus in primary hepatocellular carcinoma."

"The site of integration in the host cell DNA," he explained, "suggests a promoter insertion model for cellular transformation."

Dr. Rutter's evidence suggests that the regulatory sites on the virus somehow influence cellular oncogenes. He described the location of a "control lesion" on the gene for expression of the viral genes that are associated with replication of the DNA itself and said a separate promoter controls the surface antigen.

"Analysis of the sequences of these integrated DNAs suggests that some of those promoters may be in a position to activate the expression of post-sequence," he remarked.

Among Dr. Rutter's other achievements are the cloning and extensive study of the human insulin gene, and a major contribution to the understanding of molecular genetics of hormone action, especially the hormones that regulate carbohydrate metabolism.

NATIONAL CENTER FOR HEALTH SERVICES RESEARCH

NCHSR

BREAST CANCER SCREENING METHODS EVALUATED

Risk level —which is determined mostly be age— is the primary consideration in screening asymptomatic women for breast cancer, concludes a recent cost/benefit study funded by the National Center for Health Service Research

(NCHSR). Results suggest that most asymptomatic women under age 47 do not need regular, formal screening unless they have had intensive breast irradiation or have a family history of breast cancer, which may place them in a high-risk group. For all women over age 47, and for all high-risk women regardless of age, the study indicates that the optimal screening protocal consists of biennial (and possibly annual) examination by high-quality mammography coupled with clinical palpation. Biopsies are performed as indicated by the results of these examinations. "These fidings are only a guide to selecting the most cost-effective screening strategy," cautioned principal investigator John Kenneth Gohagan, Ph.D., of Washington University. "Study results are not meant to override a physician's clinical judgment nor to downplay the importance of monthly self-examination for all women." The study evaluated the three most-used breast cancer screening methods —mammography, thermography, and clinical examination— in terms of their specificity and sensitivity, potential radiation hazards, and the extent to which costs would be born by patients. Data for the analysis were collected from about 10,000 women over a five-year period by the Breast Cancer Detection Project No. 25 in Columbia, Missouri. Data from projects in other localities are now being examined to determine whether the conclusions are applicable throughout the country. A summary of the study results, "Benefit-Cost Evaluation of Breast Cancer Detection Strategies," is available from NCHSR. Study results are slated to be published this Spring by Praeger Publishers in *Early Detection of Breast Cancer Risk, Detection Protocols, and Therapeutic Implications.*

AMERICAN COLLEGE OF SURGEONS

WARNING ISSUED ON SURGICAL FILTER

Without attempting to analyze the complex background of the surgical complications in question, the College feels compelled to publicize, in the best interest of patients, the following note:

The Emergency Care Research Institute (ECRI) released an Urgent Hazard Bulletin dated march 5, 1982, pertaining to the Bently AF-10 arterial blood line filter. According to ECRI, the Bently AF-10 (25-micron) arterial blood line filter (Bently Laboratories, 1705 Armstrong Avenue, Irvine, CA 92714) appear associated with a higher-than-usual incidence of serious intra— and postoperative complications. A follow-up bulletin, dated April 19, 1982, indicates there is a reasonable likelihood that variations in set-up and use may have contributed to reported complcations.

For further information write to ECRI, 5200 Butler Pike, Plymouth Meeting, PA 19462, (215) 825-600.

COLLEGE PUBLISHES SECOND OPINION PROGRESS REPORT

Second Surgical Opinion Programs: A Review and Progress Report, recently published by the American College of Surgeons, updates two previous College reports on these programs and presents current information, including research results, on both private and government initiatives. Highlights of the report include:

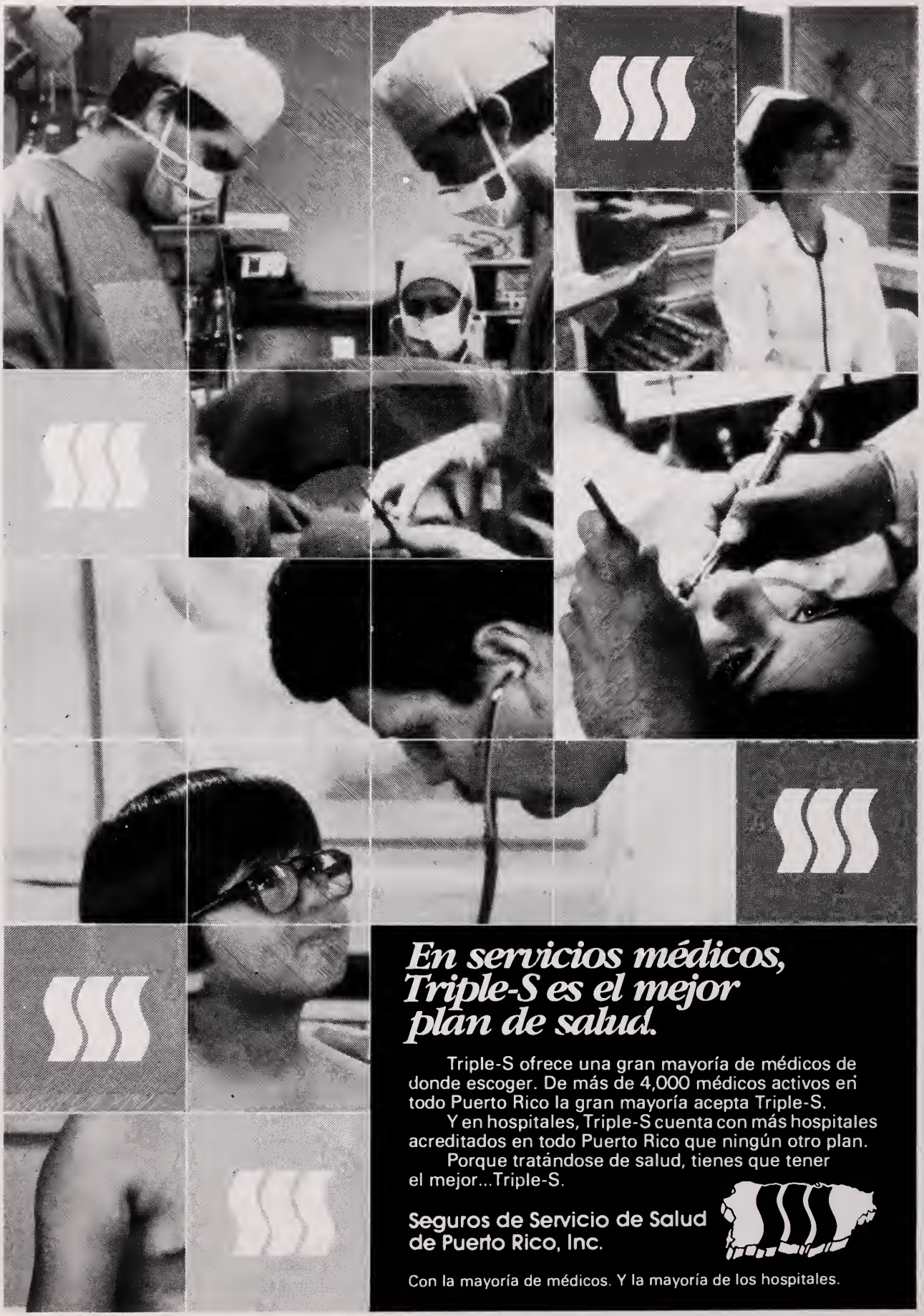
- A discussion of Cornell-New York Hospital's second surgical opinion program, the first formal program established in this country in 1972.
- Descriptions of the second surgical opinion programs sponsored by various Blue Cross and Blue Shield plans and of the Prudential Insurance Company's program.
- A review of the federally funded demonstration projects and evaluation efforts concerning second surgical opinion programs.

Available research findings, included in the report, address the following: overall usage rates, nonconfirmation rates (i.e., the rate at which the second opinion does not confirm the first opinion), patient compliance, effects of second opinion programs on surgical rates and patient outcomes, program costs and benefits, and mandatory versus voluntary programs. Some of the findings are as follows:

- Participation in voluntary programs is consistently low.
- Nonconfirmation rates in voluntary programs ranged from 30 to 35 percent; in mandatory programs, rates ranged from 5 to 19 percent.
- Patients did seem to be influenced by the second physician's recommendation, and patients who sought a third opinion generally followed that physician's recommendation.
- Mandatory programs seemed to decrease the rate at which operations were performed, while voluntary plans had a negligible effect on operation rates.
- Although mandatory programs are cited as a remedy for the failures of voluntary programs, voluntary programs are still more widely offered.

A summary of the College's views on second surgical opinion programs is also included in the report. In brief, the College has opposed mandatory programs but does not oppose voluntary second surgical opinion programs that are well planned and thoughtfully implemented.

Second Surgical Opinion Programs: A Review and Progress Report is available free of charge from the Surgical Practice Department, American College of Surgeons, 55 Est Erie St., Chicago, IL 60611.



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ASOCIACION MEDICA DE PUERTO RICO

BOLETIN

INSTRUCCIONES PARA LOS AUTORES

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

Se urge a los autores se esfuerzen en perseguir claridad, brevedad, e ir a lo pertinente en sus manuscritos no importa el tema o formato del manuscrito.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

Manuscrito

El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos en maquinilla a doble espacio; por un solo lado de cada página, en TRIPLICADO y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

Nomenclatura

Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

Tablas

Las tablas deben aparecer en hojas separadas. Estas deben incluir el título, y el número de la tabla debe estar en romano. Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla. Se usará en las tablas el mismo idioma en el cual está escrito el artículo. Deben limitarse las tablas a solo aquellas que contribuyan al mejor entendimiento del manuscrito.

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Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor. Debe indicarse en la parte superior de la ilustración.

Resumen

Un abstracto no mayor de 150 palabras debe acompañar los manuscritos. Debe incluir los puntos principales que ilustren la substancia del artículo y la exposición del problema, métodos, resultados y conclusiones.

Referencias

Las referencias deben ser numeradas sucesivamente de acuerdo a su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Deben utilizarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana. Las referencias deben seguir el patrón que se describe a continuación.

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Cartas al Editor

Se publicarán a discreción de la Junta Editora. Deben estar escritas en maquinilla a doble espacio, no deben ser mayor de 500 palabras, ni incluir más de cinco referencias.

INSTRUCTIONS TO AUTHORS

The Boletin will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the understanding that it is to be published solely in this journal.

All authors are urged to seek clarity, brevity, and pertinence in the manuscripts regardless of subject or format.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

Manuscripts

The entire manuscript, including legends and references should be typewritten double spaced in TRIPLICATE with ample margins. A separate title page should include the following: title, authors and their degrees (e.g. MD, FACP), city where the work was done, hospital or academic institutions, acknowledgement of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

Nomenclature

Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurement should be used preferentially).

Tables

These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines should be omitted. The language used in the tables must be the same as that of the article. Include only those tables which will enhance the understanding of the article. They should supplement, not duplicate the text.

Figures

Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

Summary

An abstract not longer than 150 words should accompany all articles. It must include the main points that present the core of the article and the exposition of the problem, method, results, and conclusions.

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BOLETIN

VOL. 74/NUM. 5-6 MAYO-JUNIO 1982

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COLUMNA DEL EDITOR

Este número extraordinario tiene su razón de ser: es consecuencia directa de los cuatro meses que estuvo sin publicarse el Boletín. Durante ese tiempo varias casas farmaceúticas retiraron sus anuncios, con la consecuente pérdida del ingreso que provenía de la publicación de los mismos. A pesar de muchos esfuerzos y sacrificios personales, no se materializó la publicación de un número cada dos semanas hasta lograr ponernos al día, como se había proyectado. Las causas fueron múltiples; algunas decepcionantes, otras inesperadas y muchas fuera de nuestro alcance para salvarlas.

En un esfuerzo para compensar la pérdida de estos anuncios, se ha intensificado la búsqueda de anunciantes a nivel local, aunque confesamos que ignoramos cuáles serán los resultados. Para evitar continuar perdiendo anuncios, se hicieron contactos personales con la "State Medical Journal Advertising Bureau", en Chicago, Illinois, quien representa las compañías anunciantes norteamericanas. La recepción fue buena y manifestaron su intención de ayudarnos, pero enfatizaron que la pérdida de anuncios sólo podía evitarse manteniendo el Boletín al día. Esto se tiene que conseguir para septiembre de 1982, fecha en que ellos renuevan los contratos con las compañías que desean anunciarse. En su opinión, si este objetivo se logra, ellos aseguran la recuperación de los anuncios perdidos y que con un formato nuevo y más atractivo, como el que tenemos al presente, es posible conseguir nuevos anunciantes. La única forma de poder "vencer el tiempo" es con un número extraordinario, condensando dos meses en una tirada. El precedente ya ha sido establecido por revistas de Asociaciones Médicas de algunos Estados bajo circunstancias similares a la nuestra, por lo que se aprobó unánimemente hacerlo y tocó a los números de mayo-junio y julio-agosto.

Por otro lado, nos pesa comunicar a la matrícula que à partir del último día de junio del presente año, el Sr. Primitivo Pagán, Supervisor de nuestra imprenta, se acogió a los beneficios del retiro. Durante los años que laboró para esta Asociación, el señor Pagán fue un celoso guardián de los intereses de la misma y en particular del Boletín. Creemos que si nuestro Boletín aún existe, a pesar de tanto obstáculo, y ha llegado a ser lo que es al presente, se debe en gran medida a su labor. La Junta Editora del Boletín de la Asociación Médica de Puerto Rico quiere hacer público su reconocimiento a la labor del señor Pagán, le da una vez más las gracias y le desea salud para que pueda disfrutar su retiro por muchos años.

Rafael Villavicencio, M.D.
Presidente, Junta Editora
Boletín Asociación Médica de Puerto Rico

NUESTRA PORTADA

"Bodegón Puertorriqueño" oleo por Ricardo Ramírez Palacios.

El autor es nacido en Santurce, Puerto Rico en 1958 y a temprana edad se muda a Nueva York. Hace un bachillerato en Artes con concentración en Pintura en la Universidad del Estado de Nueva York y se traslada a la isla a principios de 1982. Con anterioridad sus obras habían sido expuestas en: Jascha Giller Bookstore and Gallery en Nueva York y en el Mamaroneck's Artist's Guild Exhibition de 1981, también en Nueva York. Localmente sus obras han sido expuestas en la Galería San Sebastían y Galería Las Palomas en el Viejo San Juan, así como en el Taller Galería André en Hato Rey.

Las obras de este joven artista ya comienzan a ser comentadas por los entendidos en pintura de una forma muy positiva. Ven en el joven Ramírez un gran talento con muchas probabilidades de figurar entre los más destacados exponentes de las Artes Plásticas nacionales.

En el óleo que aparece en nuestra portada el artista logra armonizar las imágenes sobrias de los clásicos bodegones con el alegre colorido de las figuras de los Reyes Magos que tan hábilmente son esculpidas por nuestros artesanos.

La Asociación Médica de Puerto Rico le dá las gracias al artista y al Taller-Galería André en el Condominio El Centro, de Hato Rey por cedernos la obra para su reproducción en nuestra portada.

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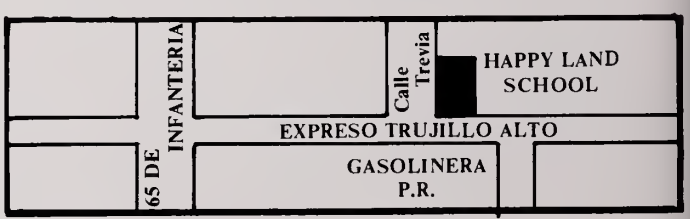

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Reference: 1. Finnerty, F.A., Jr.: Hypertension: The Continuing Challenge, Scientific Exhibit, Meeting of the AAFP, Boston, Mass., Sept. 20-23, 1976.

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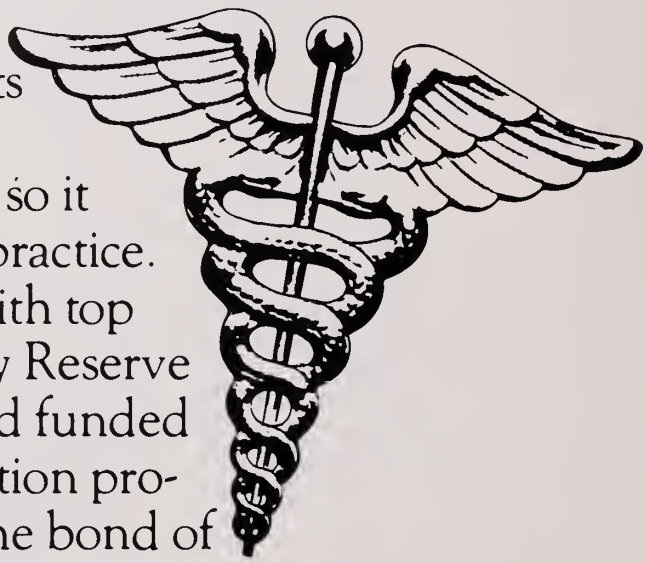

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CONTENIDO

EDITORIAL

Chronic Nonspecific Diarrhea of Infancy

The review article on chronic nonspecific diarrhea (CNSD) of infancy by Dr. E. Cichowicz represents a worthwhile effort to bring to the medical practitioner recent clinical and experimental experience with this problem. Chronic nonspecific diarrhea of infancy is a disease in which biological, medical and social factors play important roles. It is a disease of the bottle-fed infant, and is believed to be related to penetration of food antigens through the small bowel mucosa. However, as pointed out by Dr. Cichowicz, antigen penetration is up to a certain level physiological in the developing small bowel. Thus it has been suggested that the magnitude of the antigenic load at the small bowel sites, as well as a certain undefined immunogenetic make up, may also be essential for the immunological expression of antigen absorption. While the importance of such pathogenetic factors is still hypothetical, secondary factors are known to play a critical role in the severity and possibly also in the duration of the disease. One such factor is intestinal infection, especially by enteroviruses, which is oftentimes responsible for exacerbations of the diarrhea. Another factor is the misconception on the part of the physician that the problem can be solved by changing the formula. This misconception is transmitted to the child's mother, and when this dietary manipulation fails, the result is a feeling of deception and distrust. We teach our fellows and housestaff that a critical aspect in the management of infantile CNSD is the patient's mother's understanding of the nature of the disease and of the importance of maintaining an adequate nutrition. The mother's concern must be shifted from the diarrhea symptom, as upsetting as it can be, to the body weight and growth status of the child. When this is achieved it is then possible to focus on the nutritional management of the problem. Dr. Cichowicz's emphasis on this point is quite appropriate.

In some way, CNSD occuring during the lactating period in the bottle-fed infant may ultimately represent an extreme clinical expression of the absence of the trophic effect of breast milk. Maternal milk, particularly colostral milk, contains not only immunological components, but also a great variety of factors that probably promote and modulate the growth and maturation of the bowel. The high content of epidermal growth factor (EGF) and the high specificity of the milk fat globule glyconjugates in human breast milk are good examples of the potential trophic properties of breast feeding. The combined activity of breast milk hormonal and substrate components might be important, among other things, in establishing the permeability barrier of the mature bowel mucosa. New information in this field will indeed help to improve our understanding of the antigenic properties of artificial formula feeding and their potential clinical consequences.

Ramón Torres-Pinedo, M.D.
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ESTUDIOS CLINICOS

Percutaneous Needle Biopsy of the Lung

David Figueroa, MD
Antonio J. Grillo-López, MD
Cesar Soto-Gautier, MD
María Castillo-Staab, MD

Summary **Percutaneous needle biopsy of the lung produced histologic confirmation of malignancy in 15 of 18 patients (83%) with suspected lung cancer. Most patients had peripherally located lesions and all except one had negative sputum cytology. Pneumothorax occurred in five patients: one patient required chest tube insertion, another required catheter aspiration, and three needed no treatment. A review of pulmonary needle biopsy and its role in the diagnosis of lung cancer is presented.**

Cancer of the lung annually accounts for 9.5% of all new cases of cancer in Puerto Rican men.[1] It presently ranks second in incidence to cancer of the prostate; the annual number of new cases per 100,000 Puerto Rican men is 27.4 for prostatic cancer, 16.3 for lung cancer, and a closely-ranked 16.1 for stomach cancer. Lung cancer has steadily increased in incidence over the past fifty years and it remains a leading cause of cancer mortality in Puerto Rico.[1] Over 90% of the cases of squamous and oat cell lung cancer in men are related to cigarette smoking.[2]

The prognosis for lung cancer is poor and its management is a formidable challenge even with improved modalities of treatment.[3,4] At the time of diagnosis, aproximately 70% of all patients are inoperable, and of the remaining 30%, the tumor will be unresectable or partially resectable in 15% and completely resectable in the other 15%. Only 4% of the patients (all from the latter group) will be alive and free of disease after five years.[4]

Diagnosis during the early localized stages clearly improves therapy and survival.[5] In the operable cases, a tissue diagnosis is obtained at thoracotomy. In the inoperable patient, histologic confirmation can be obtained by various means including sputum cytology, lymph node biopsy, bronchoscopic biopsy, and others. Even so, in Puerto Rico 28% of all cases lack histologic confirmation which might in part explain why 30% of all patients die untreated.[1]

Percutaneous needle biopsy of the lung is a diagnostic procedure which in selected cases may be of value. It is a procedure infrequently used in Puerto Rico but one which appears to offer valuable diagnostic support in the inoperable patient with a pulmonary lesion. Our experience with this procedure and a discussion of its use in the diagnosis of lung cancer are presented.

Materials and Methods

Eighteen patients, fourteen men and four women, were admitted to the Metropolitan Hospital with radiographic evidence of pulmonary lesions suggestive of neoplasia. The patients ranged in age from 52 to 88 years with a mean of 71 and a median of 73 years. Chest x-ray, bone survey, and routine laboratory studies were performed in all cases. Special studies such as tomography and nuclear scans were done when indicated.

Biopsy Procedure

The lesion was localized radiologically by anteroposterior and lateral chest films. Frontal and lateral tomograms of the chest were also done if necessary for more accurate localization. The depth of the lesion was measured directly on these films. Fluoroscopy was performed with the patient in the position selected for biopsy and the site of puncture was marked on the skin. The patient was then taken to the operating room where he was prepared and draped in the usual fashion and positioned exactly as during fluoroscopy. Under 2% local lidocaine anesthesia, a small stab wound was performed at the site of skin puncture. A Vim-Silverman needle was introduced to the predetermined depth and a biopsy specimen obtained. The procedure could also be done in the fluoroscopic table and the needle introduced under intermittent fluoroscopic control to guide the needle path. A chest film was taken after the procedure for the control of possible pulmonary hemorrhage, pneumothorax, pneumomediastinum, or subcutaneous emphysema.

Results

The eighteen patients had lesions which in most cases were peripherally located: five were RUL, ten LUL, two L midlung, and one RLL. Except for one sputum specimen "strongly suggestive of keratinizing squamous cell CA," all serial sputum samples for cytology were negative. Percutaneous needle biopsy of the lung, however, produced histologic

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confirmation of malignancy in 15 cases (83%). Twelve of these patients had definitive evidence and three had suggestive evidence of lung cancer; in three patients the specimens were nondiagnostic (Table I). Eight of the twelve patients with confirmed lung cancer had an epidermoid malignancy.

punctures to the lesion center had yielded only necrotic tissue.

Pneumothorax, subcutaneous emphysema, and pain were the only complications (Table 2). One patient with a partially collapsed left upper lobe had a large (50%) pneumothorax which required insertion of a thoracostomy tube. Another

TABLE I

Diagnostic Yield of Percutaneous Needle Biopsy of the Lung

	No. Patients	Percent
Preoperative Diagnosis of Long Cancer	18	100
Histologic Diagnosis by Needle Biopsy		
I. Confirmed Lung Cancer		
Epidermoid	8	44
Adenocarcinoma	3	17
Anaplastic	1	5
II. Suggestive of Lung Cancer	3	17
TOTAL	15	83
III. Nondiagnostic	3	17

Histologic specimens recovered by needle biopsy are illustrated for bronchogenic carcicoma (Figure 1) and for a poorly differentiated squamous cell carcinoma (Figure 2) and adenocarcinoma (Figure 3) of the lung. An example of a lesion which was not peripherally located but was amenable to needle biopsy is shown in one patient (Figures 4 and 5). Despite the tumor's location near the hilar area and proximal to bronchi, large blood vessels, and lymph glands, the lesion was successfully biopsied.

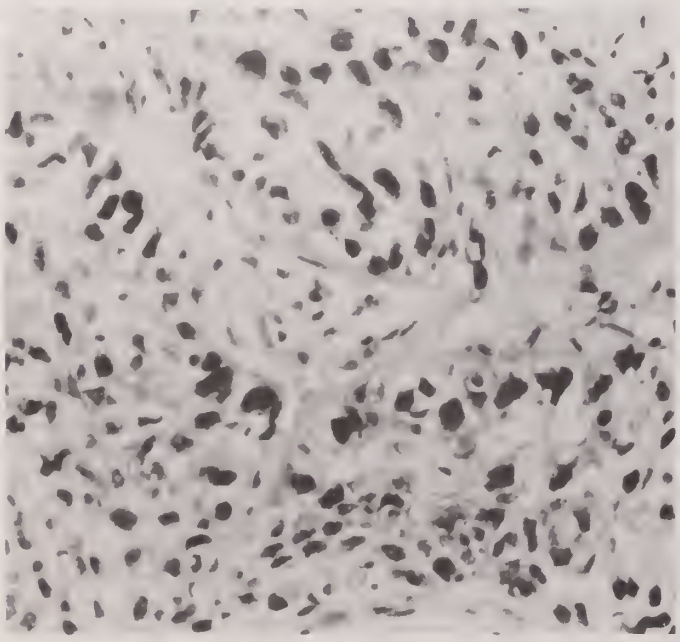

Fig. 1. Bronchogenic carcinoma. (Hematoxylin and eosin.)

Precise positioning of the needle was possible and greatly improved the diagnostic yield. The precision was of little benefit for one patient, however, who was found to have a mucin-producing adenocarcinoma at thoracotomy but whose prior needle biopsies had not been diagnostic because

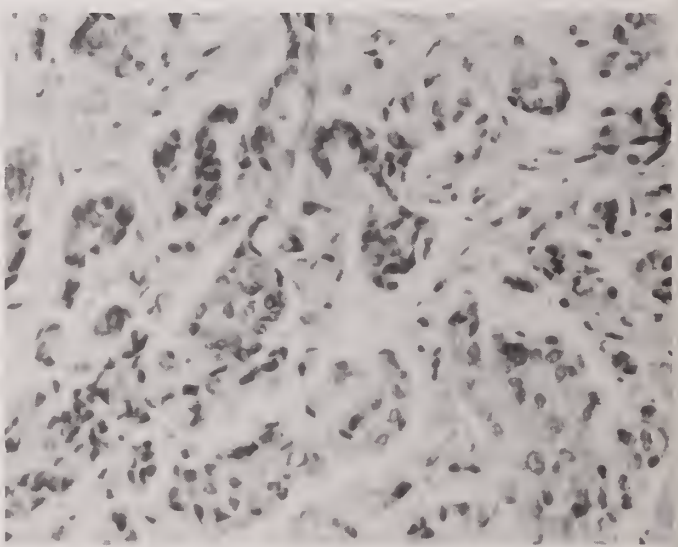

Fig. 2. Poorly differentiated squamous cell carcinoma of the lung. (Hematoxylin and eosin.)

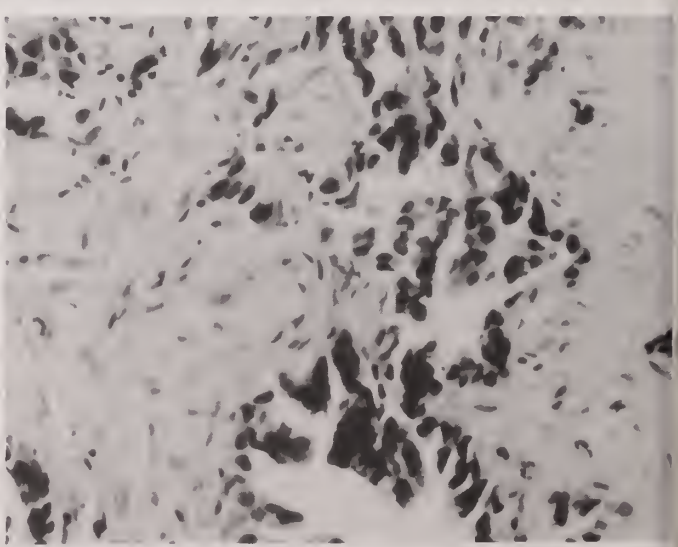

Fig. 3. Poorly differentiated adenocarcinoma of the lung. (Hematoxylin and eosin.)

Fig. 4. Large lesion in right hilar area. (Right lateral tomographic cut.)

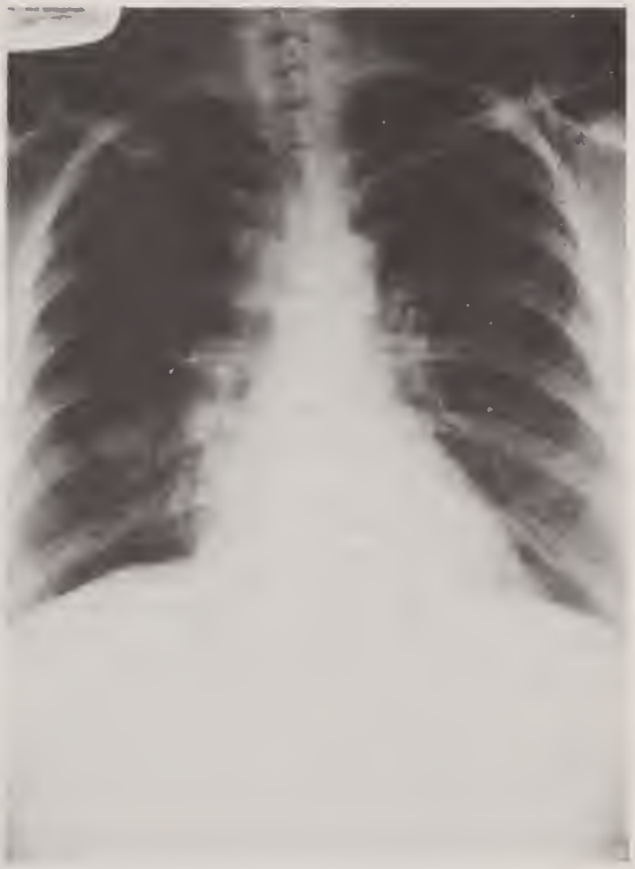

Fig. 5. Same lesion. (Anteroposterior radiography).

patient had a 30% pneumothorax which was easily managed by aspiration through an intracatheter inserted in the pleural space. Three other patients had minimal pneumothorax which required no specific treatment and resolved spontaneously.

Discussion

Once lung cancer is suspected, histologic confirmation must be obtained early to assure prompt, appropriate

TABLE II

Complications of Percutaneous Needle Biopsies of the Lung

	Complication	Possible Predisposing Factors	Treatment
Case #13	Pneumothorax (50%)	Partially collapsed LUL	Chest Tube
	Subcutaneous Emphysema	Cavitation within lesion	
	Pain	Mediastinal shift	
Case #5	Pneumothorax (30%)	Pulmonary vascular congestion	Intra-catheter
	Pain	Congestive heart failure	
		Cardiomegaly	
Case #3	Pneumothorax (minimal)	Emphysema	None
Case #1	Pneumothorax (minimal)	Fibroemphysema	None
Case #10	Subcutaneous Emphysema		
	Pneumothorax (minimal)	None	None

treatment. In patients with abnormal x-ray films, three methods of lung biopsy are avialable: open surgical, percutaneous needle, and bronchoscopic, the latter making use of the rigid or fiberoptic bronchoscope to obtain specimens from biopsy, brushing, or washing. The most definitive procedure is open biopsy which allows larger, more representative samples but involves more extensive surgery and is often contraindicated by the patient's poor condition and stage of disease and the availability of other diagnostic techniques. Fiberoptic bronchoscopy is a routinely-used procedure for visualizing lesions and obtaining specimens for histologic examination. Its utility, however, is restricted to lesions on or near accessible segmental and subsegmental bronchi. Percutaneous needle biopsy is a valuable procedure for obtaining biopsies of peripheral lesions in the lung parenchyma, particularly those near the chest wall.

The history of needle biopsy of the lung dates back to the late 1800s. In 1886, Menetrier apparently made the first diagnosis of lung cancer with aspiration lung biopsy.[6] By 1936 over 2000 cases had been reported in the literature with only one mortality. In 1959 Sarin and Bhatnagar introduced the use of the Vim-Silverman needle for lung biopsy.[7] A year later, Sabour and others reported 137 biopsies following this technique with only six patients experiencing complications.[8] Over the past two decades a large amount of experience has been gained and many consider percutaneous needle biopsy the diagnostic procedure of choice for the peripherally located, solid, small pulmonary lesion.

In order to avoid complications one must carefully note that there are indications and contraindications to this procedure. The specific indication is the peripherally located pulmonary lesion which cannot be diagnosed by more conservative methods such as sputum cytology, biopsy of palpable lymph nodes, etc. Contraindications include: a) poor patient cooperation —the patient must be able to hold his breath and cannot have uncontrollable cough; b) presence of cysts or bullae in the area to be biopsied; c) clinical evidence of significant pulmonary hypertension; d) poor cardiopulmonary reserve; and e) bleeding disorders.[9]

Percutaneous needle biopsy permits direct approach to localized pulmonary lesions with a high degree of accuracy. Diagnostically accurate cytological determinations range in recent studies from 72 to 97% and a yield of 80% or better is usually achieved.[10-17] The incidence of pneumothorax in the cited studies ranged from 8 to 44% and hemoptysis from 2 to 16%. In a large study involving 5300 needle biopsies of the lung in 2,726 patients, a cytological diagnosis was established in 91% of the patients; pneumothorax, which usually required no treatment, occurred in 27% and hemoptysis was noted in 2-5%.[15] In another large series of over 1,000 patients undergoing thoracic needle biopsies, 60 of whom had duplicate biopsies, the overall diagnostic accuracy was 87% and the complications of pneumothorax and hemoptysis were, respectively, 14% (3% requiring treatment) and 2.3%.[16]

Needle biopsy is more accurate in obtaining tissue than is bronchoscopy particularly when lsesions are 2 cm or less.[12] Since small peripheral tumors of less than 2 cm appear to have the best prognosis,[18] good diagnostic yields from these lesions are essential. In a study of 367 patients with lung cancer, Hayata and coworkers[19] compared the diagnostic yields of needle biopsy with rigid and fiberoptic bronchoscopy. Needle biopsy provided better diagnostic yields than did the other methods, with a rate of 75% for lesions of 2 cm or less and 89.6% for lesions of greater than 2 cm. Brushing cytology was positive in 66.7% of lesions 2 cm or less and in 59.6% of lesions greater than 2 cm. Sputum cytology was positive in only 21.7% of the cases when lesions measured 2 cm or less. Berquist et al[12] obtained a positive tissue diagnosis by needle biopsy in 68% of lesions less than 2 cm in 86% of lesions larger than 2 cm. In the study by Hayata et al,[19] the diagnostic yield using fine needle aspiration under televised image-intensified fluoroscopy was comparable to the 83% yield obtained in our study without fluoroscopic guidance and with less sophisticated techniques.

The wide ranges in frequency of complications noted earlier were accounted for partly by technical variations, but principally by the variable compositions of the study groups. Many patients had malignant disease, were older with poor lung recoil, and were in poor health; many were not candidates for surgery but required tissue diagnosis before institution of chemotherapy. In these patients the incidence of pneumothorax was much greater, particularly when cavitating and mediastinal lesions were present, while in clinically stable patients under 50 years old, the incidence of pneumothorax was approximately 10%.[12] The number of needle passages and the needle diameter also affected the incidence. In the vast majority of cases, the penumothorax is small and self-limited and may be handled with no therapy or with simple aspiration procedures; approximately one out of 20 patients, however, requires surgical insertion of a chest tube, a procedure practiced routinely in most open-lung biopsies.[20] As with pneumothorax, hemoptysis occurred more frequently in older, debilitated patients and in those with lessions close to central blood vessels, or with infiltrative and cavitating lesions rather than solid nodules.[12]

If a thin needle is used and careful fluoroscopic procedures are followed, the complication rate for needle biopsy of centrally located, hilar and mediastinal lesions need not exceed that for more peripheral lesions.[17] A major concern, that of metastatic seeding along the needle tract, is rarely encountered. It has been reported only once in studies employing aspiration biopsies with hollow needles[21] and twice in all published series employing Vim Silverman needles.[22 23]

Conclusions

The results of our study in a small number of patients parallel those obtained in larger studies. In our experience, percutaneous needle biopsy in the diagnosis of lung cancer affords the same advantages as those reported by others. These are summarized briefly below.

Since early diagnosis allows better prospects of prompt, appropriate therapy, the use of needle biopsy in suspected lung cancer is gaining acceptance as a minor, inexpensive, and safe procedure with a high diagnostic yield that compares favorably with fiberoptic bronchoscopy. Positive tissue diagnoses of 80% or better are often obtained. The procedure can be readily performed in hospitals with minimal x-ray facilities. It is completed in a few minutes and is easier to perform and involves much less patient discomfort than bronchoscopy and bronchial brushing.[16] In addition, needle biopsy can be performed on an outpatient basis and the results of cytological examination can be obtained in two hours or less compared with the one or two days required for histologic sections.[13] Such facilitation allows the physician to plan therapeutic

approaches earlier and more efficiently, and to perhaps obviate further diagnostic efforts. A big advantage of percutaneous needle biopsy is its safety. Although the procedure carries an inherent risk of pneumothorax and hemorrhage, the complications by and large are minor and easily managed and the risk of needle biopsy is well outweighed by the therapeutic gain.[24]

Resumen: La biopsia percutánea del pulmón resultó en evidencia histológica de malignidad que confirmó el diagnóstico en 15 de 18 pacientes en quienes se sospechaba cáncer del pulmón. Los pacientes tenían lesiones localizadas periferalmente y 17 de 18 tenían citología (del esputo) negativa. Cinco pacientes tuvieron pneumotorax: uno requirió tubo de pecho; otro requirió aspiración vía cateter; y tres no necesitaron tratamiento alguno. Se presenta un repaso del rol de la biopsia percutánea del pulmón en el diagnóstico del cáncer del pulmón.

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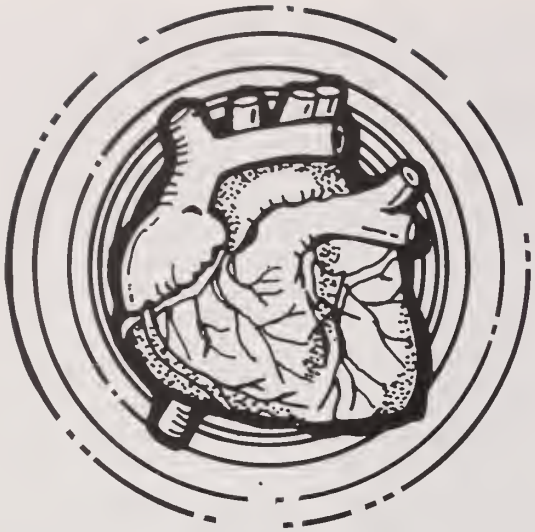

Métodos Diagnósticos del Infarto del Miocardio en el Paciente Sometido a Cirugía Aorto-Coronariana

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El diagnóstico de infarto del miocardio en el período post-operatorio inmediato en pacientes sometidos a cirugía abierta del corazón y puentes aortocoronarios sigue siendo una difícil tarea y en ocasiones controversial. El objetivo primordial de esta intervención quirúrgica es el de aliviar síntomas anginosos y en algunos casos, prolongar la vida,[1] esto último a través de la disminución de infartos de miocardio y la preservación de la función normal del músculo cardíaco. Para evaluar la efectividad de la cirugía en la preservación del músculo cardíaco y la presencia o ausencia de necrosis aguda de tejido miocárdico, se han utilizado diversas pruebas diagnósticas con variados resultados individuales. Fennell[2] Raabe[3] y Righetti[4] han recomendado la combinación de pruebas diagnósticas para obtener mayor sensitividad y especificidad.

El propósito de este estudio es la evaluación prospectiva de la sensitividad y especificidad relativas del electrocardiograma, (ECG), la fracción muscular cardíaca de la enzima creatina-fosfoquinasa (CPK-MB), y la cintigrafía cardíaca con el radio-nucleido pirofosfato de tecnesio (TcPyp), en el dianóstico temprano del infarto de miocardio perioperatorio en pacientes sometidos a cirugía aorto-coronariana.

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Materiales y Métodos

Desde junio del 1980 a marzo del 1981, cincuenta y dos pacientes fueron sometidos a cirugía de puentes aorto-coronarios en el Hospital de Veteranos en San Juan, Puerto Rico. Todo paciente con afección valvular fue rechazado para el estudio. Cuarenta de los cincuenta y dos pacientes fueron aceptados para el estudio.

A todos los pacientes se les hizo electrocardiogramas de superficie de doce derivadas el día antes, inmediatamente en el período post-operatorio y diariamente por tres días consecutivos después del procedimiento quirúrgico. Los criterios usados para el diagnóstico de infarto de miocardio agudo transmural fueron la presencia de una onda Q nueva de por lo menos cuarenta milisegundos de duración en dos o más electrodos adyacentes (4). Disminución de la onda R en un área sin presencia de una onda Q nueva no fue considerado diagnóstico de infarto del miocardio. (Tabla I).

TABLA I

Métodos	
A. ECG-	antes de cirugía y diario por tres días luego de cirugía
	*Nueva onda Q >.04 segundos
B. CPK-MB-	6,24 y 48 horas luego de cirugía
	*8% del CPK total
C. Tc-PyP-	tan pronto sea posible luego de cirugía
	*Captación focal Costillas (2+)

* Criterios de una prueba positiva

Se tomaron muestras de sangre para la determinación cuantitativa de CPK total y fracción miocárdica (MB) antes de la cirugía y a las 6, 24 y 48 horas luego de la cirugía[5]. La presencia y cuantificación del CPK total y su fracción MB fueron determinados usando la técnica de electroforesis con acetato de celulosa y por examen de fluorescencia con la lámpara de Woods[6]. Su cuantificación por densitometría fue llevada a cabo con el método de "Helena Clini-Scan Densitometer"[7]. Se consideró indicación de infarto de miocardio cuando la fracción MB fue igual o mayor que el 8% del CPK total[5]

La prueba de pirofosfato de tecnesio 99-m fue hecha tan pronto fue posible post-operatoriamente y esto fue entre el segundo y el onceavo día, con una media de siete días. Una prueba positiva fue considerada si había captación definitiva y focal en el área cardíaca mayor o igual a la intensidad con que captaban las costillas[8 9 10]. No se consideró diagnóstico de infarto una captación difusa del miocardio. Se consideró diagnóstico de infarto de miocardio cuando dos o más de

estas pruebas eran positivas de acuerdo a la clasificación de Raabe y colaboradores[3].

La sensitivdad de una prueba se definió como el porcentaje de pacientes con enfermedad que son detectados correctamente por la prueba.[11]

$$\frac{\text{Positivos verdaderos}}{\text{Positivos verdaderos + falsos negativos}}$$

La especificidad de una prueba se definió como la habilidad de una prueba negativa de identificar correctamente a individuos normales.

$$\frac{\text{Negativos verdaderos}}{\text{Negativos verdaderos + falsos positivos}}$$

El valor predictivo de una prueba anormal es el porcentaje de pacientes con una prueba anormal el cual es indicativo de enfermedad.

$$\frac{\text{Positivos verdaderos}}{\text{Positivos verdaderos + falsos positivos}}$$

Las características del grupo fueron las siguientes: (TABLA II)

Todos los pacientes eran varones con una edad promedio de 54 años. El 80% tenían enfermedad de tres vasos coronarios y solo el 20% tenían enfermedad de 1 ó 2 vasos. En 65% de los pacientes se hizo revascularización completa. Se construyeron un promedio de 2.7 puentes aorto-coronarianos por paciente.

El tiempo de bomba (circulación extracorpórea) y abrazadera aórtica, fue similar en todos los pacientes (aproximadamente 2 a 3 horas). En todos se paralizó el corazón con el sistema de cardioplegia fría y se colocó un sistema de succión en el ventrículo izquierdo. Luego se reanimaba con defibrilación eléctrica.

En todos los pacietnes se hicieron electrocardiogramas seriados y en treinta y cinco pacientes se obtuvo un mínimo de dos muestras de CPK-MB post-operatoria. Solamente en veintitrés pacientes se pudo hacer el cintigrama con radio nucleido.

TABLA II

Características Clínicas	
Número de pacientes	40
Edad promedio	54(34-72)
Número de vasos coronarianos afectados: (lesión obstructiva mayor de 50%)	
1	3 (8%)
2	5 (12%)
3	32 (80%)
Número de puentes por paciente	2.7
Revascularización completa	26 (65%)

Resultados

Catorce de los 40 pacientes (38%) demostraron la presencia de una Q nueva en dos o más derivadas en los electrocardiogramas de superficie obtenidos después del procedimiento quirúrgico. De los 35 pacientes que tuvieron determinaciones de la enzima CPK total y la fracción miocárdica (MB), 10 tuvieron valores de la fracción miocárdica mayor de 8% del CPK total. Veintitrés pacientes tuvieron cintigramas con pirofosfato de tecnesio después del procedimiento quirúrgico. Tres de éstos tuvieron captación que fue considerada positiva para infarto del miocardio.

Utilizando solamente los veinte pacientes en que se hicieron las tres pruebas diagnósticas, la Tabla III demuestra los resultados obtenidos. Cinco de los veinte pacientes tuvieron infarto peri-operatorio de acuerdo a los criterios previamente definidos. La sensitividad más alta se obtuvo con el electrocardiograma de superficie (5/5). La prueba más específica y predictiva lo fue el cintigrama con radioisótopos, sin embargo fue poco sensitivo. La prueba con isoenzimas de CPK fue poco sensitiva y relativamente la menos específica. Un gran número de pacientes obtuvieron valores altos de CPK-MB (8%) sin otra evidencia de infarto de miocardio.

TABLA III

Valor Relativo de los Tres Métodos Diagnósticos

	CPK-MB (20)	ECG (20)	TcPyP (20)
Sensitividad	40% (2/5)	100% (5/5)	60% (3/5)
Especifidad	73% (11/15)	93% (14/15)	100% (17/17)
Valor predictivo	33% (2/6)	83% (5/6	100% (3/3)

El electrocardiograma demostró siempre onda Q nueva en todos los pacientes con infarto agudo y solamente en un paciente apareció onda Q en un área que previamente no existía (pared inferior), pero que al revisar su ventriculograma pre-operatorio demostró hipoquinesia inferior. Esto posiblemente explique la presencia de la onda Q en los derivados electrocardiográficos correspondientes a la pared inferior del ventrículo izquierdo en uno de nuestros pacientes sin elevación de la enzima CPK-MB y sin captación miocárdica de pirofosfato[12 15].

Discusión

En nuestra experiencia, la presencia de una nueva onda Q luego de cirugía aorto-coronariana fue la prueba más sensitiva para el diagnóstico de infarto de miocardio peri-operatorio.

Basan y colaboradores[12] demostraron que la presencia de una onda Q en la pared inferior del corazón no es necesariamente evidencia de muerte de tejido. En pacientes con infartos previos inferiores en los cuales desaparecen con el tiempo las ondas Q, la revascularización de un área isquémica de la pared anterior del ventrículo izquierdo puede desenmascarar la onda Q inferior correspondiente al infarto previo. En todos los pacientes con nuevas ondas Q, éstas persistieron en el

trazado electrocardiográfico. La especificidad del electrocardiograma fue buena y el valor predictivo, aceptable. Esto concuerda con los estudios de Steinberg y colaboradores[12] y el grupo de Righetti y colaboradores[4] .La presencia transitoria de ondas Q patológicas durante o luego de cirugía, se ha documentado durante la oclusión aórtica o durante el inicio de la circulación extracorpórea. Estas ondas Q patológicas usualmente desaparecen poco tiempo después de restablecerse el flujo coronario indicando que su presencia no fue debido a daño miocárdico permanente[15].

Una pruea positiva con Tc-PyP es la más específica con una sensitividad moderada para el diagnóstico de infarto del miocardio después de cirugía de corazón abierto. Se han reportado pruebas falsas positivas con pirofosfato, mayormente de captación difusa, en pacientes con angina inestable, pericarditis aguda, cardiomiopatía y pacientes con aneurismas o válvulas severamente calcificadas[13-16]. En nuestro estudio no tuvimos ningún caso de cintigrafía falsamente positiva. Es decir, todos aquellos pacientes con cintigrafía de pirofosfato anormal, tuvieron elevación de la isoenzima MB y/o la presencia post-operatoria de ondas Q patológicas. La baja sensitividad del pirofosfato fue causada por el tiempo transcurrido entre la cirugía y la prueba. Se sabe que de 24 a 72 horas luego de la cirugía es el tiempo más adecuado para hacer la prueba con pirofosfato debido a la alta afinidad de éste por el tejido necrótico[16]. Estudios previos han demostrado que a partir del 6to día luego del insulto operatorio, disminuye dramáticamente la positividad de esta prueba diagnóstica, aumentando la incidencia de falsos negativos[17]. El promedio de días de espera post-operatorio de nuestros pacientes fue de siete días por lo que se explica la falla en el diagnóstico de tres pacientes con infarto miocárdico agudo. El cintigrama con pirofosfato fue la prueba de mayor valor predictivo.

La prueba que menos contribuyó al diagnóstico lo fue el CPK-MB. Su sensitividad y especificidad fueron realmente bajas. Reportes previos han demostrado que existen múltiples variables en la determinación del CPK-MB, los cuales afectan los valores obtenidos. Righetti y colaboradores[4], Raabe y colaboradores[3] y Bour y colaboradores[5] demostraron que la técnica de electroforesis es poco específica y muy variable, siendo el método de cromatografía de columna el más confiable[18-24]. La fracción MB puede ser afectada por las manipulaciones del corazón durante la cirugía, la incisión y succión por daño difuso sub-endocárdico o infartos no transmurales, lo cual puede causar aumento de esta isoenzima sin que se desarrollen ondas Q nuevas o captación de pirofosfato[25]. Otra posibilidad es la liberación de isoenzimas similares de los músculos esqueléticos[26-28].

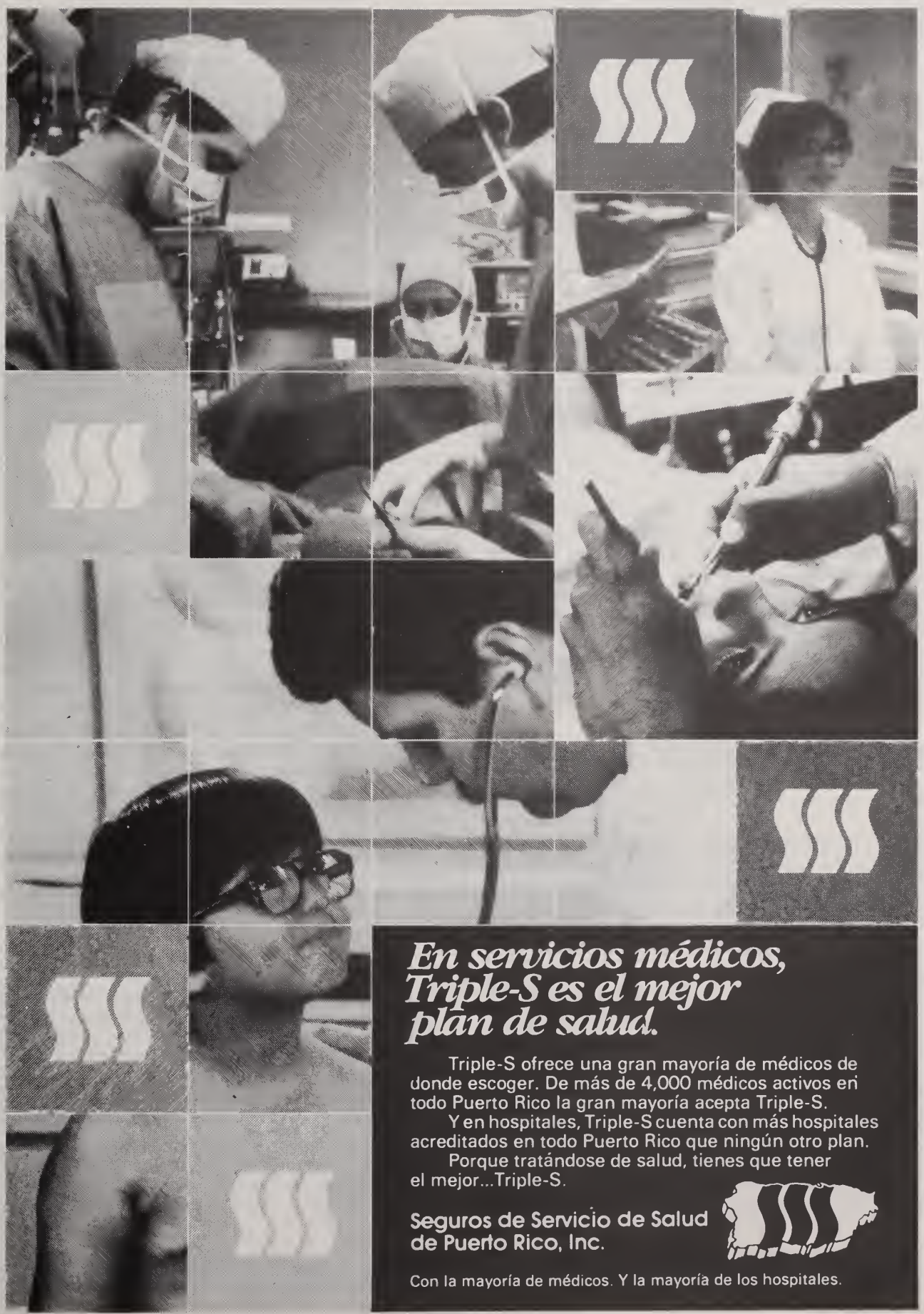
Se han utilizado otros métodos diagnósticos como las isoenzimas de LDH, SGOT, vectocardiografía, talio al descanso, pero sus utilidades no superan las pruebas antes mencionadas en este estudio[25-27].

En resumen, el uso del electrocardiograma de superficie y del cintigrama con pirofosfato de tecnesio son las dos pruebas de mayor utilidad para el diagnóstico temprano de infarto de miocardio peri-operatorio[29]. El electrocardiograma, por su alta sensitividad puede usarse como prueba preliminar y el cintigrama como prueba confirmatoria en aquellos pacientes en los que se sospeche infarto del miocardio después de cirugía cardíaca. El uso de CPK-MB por electroforesis no contribuyó significativamente en la detección del infarto perioperatorio.

Reconocimiento

Queremos agradecer a Arleen López y a Sally Rodríguez su colaboración en la preparación de este manuscrito.

(Las referencias serán suministradas por pedido al autor.)



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Pancreatitis vs. Rejection in Human Pancreatic Transplantation Unresolved Pathological Findings

Luis H. Toledo-Pereyra, MD., Ph.D.
Jerry R. Baxter, MD
Sajal Choudhury, MD
Vijay K. Mittal, MD

Abstract: **The pathological findings of five transplanted pancreas allografts are discussed in this work. Chronic rejection and pancreatitis were the main findings seen in this group of pancreases. Arterial and venous thrombosis, interlobular and perilobular fat necrosis, interlobular and perilobular fibrosis with round cell infiltration, and intimal tichkening were common findings. Acute and chronic inflammatory cells were noted in all the specimens obtained several weeks post-transplantation. The differential diagnosis of rejection and chronic pancreatitis was difficult without the clinical history. In general, rejection changes were present in all specimens, and chronic pancreatitis was associated with rejection only in the specimens obtained several weeks (more than four) after transplantation. The study of these pathological specimens offer some help in the better understanding of the acute and chronic changes occuring after pancreatic transplantation. Also, it would allow for early recognition of the immunological pancreatic allograft response at various intervals after transplantation.**

Pancreatic transplantation has been clinically performed in an attempt to stop or delay the appearance of secondary complications in patients with insulin dependent diabetes mellitus.[1-8] In this work, we studied the pathological findings of segmental pancreatic transplants removed at various intervals after grafting into insulin dependent diabetics with definitie evidence of secondary complications.

Clinical Materials and Results

The clinical material consisted of five patients who received segmental cadaver pancreatic transplants at Mount Carmel Mercy Hospital between March 3, 1980 and July 7, 1980. The operative procedure consisted of segmental pancreatic transplantation (SPT) placed extraperitoneally into the right iliac fossa. The pancreatic duct was plugged with 1-2 ml of cyanoacrylate. Approximately 60 to 75% of the pancreas was transplanted, and it consisted of the whole body and tail with or without part of the neck. The cut surface of the body or neck of the pancreas was oversewn with interrupted 3-0 vicryl suture. The vascular anastomoses were end-to-side splenic artery to external iliac artery with continuous 6-0 prolene and end-to-side splenic vein to external iliac vein with continouos 5-0 prolene. An arteriovenous fistula between the distal splenic artery and vein was selectively performed in two patients (SPT-2 and SPT-4). Immediately after transplantation, a sharp decrease in plasma glucose with no requirements of insulin indicated good pancreatic function. Rejection was considered when a sudden elevation of plasma glucose (above 175 mg%) was observed for one or two days, without returning to normal limits. Postoperatively, all patients received azathioprine, prednisolone and Minnesota antilymphoblast globulin (ALG) in a protocol similar to the one utilized for cadaver kidney transplantation.[9] Antirejection treatment, in general, was also similar to the one utilized for kidney transplantation, that is antilymphoblast globulin (ALG) was used for a period up to ten days at a dosage of 10-20 mg/k/day. In two cases, however, minimal increases of oral prednisolone and/or intravenous methylprednisolone (250 mg) were used. Pancreatic graft irradiation (150 r daily x 3) was also utilized in two patients. If the plasma glucose reached levels above 300 mg%, coverage with regular insulin was started. The pancreas allograft was removed if complete rejection and loss of function was demonstrated.

Echographic evaluation of the pancreas allografts was done using ultrasound techniques,[10] two to five days postoperatively, then every five to seven days for the first three weeks. Thereafter, ultrasound studies were performed every two to three weeks dependent on the clinical status of the transplanted pancreas. Rejection and/or deterioration of function necessitated more frequent evaluation. Subsequent to the first week after transplantation, there was a good correlation between the echographic internal structure of the pancreas and its function. However, using ultrasound techniques the development of pancreatitis could not be separated from rejection in this series.

Radionuclide examination was also done on the pancreas transplants using ^{75}Se-selenomethiomine imaging.[11] This technique wich was used to assess pancreatic function in the first weeks after transplantation, gave good correlation with organ function. Angiographic assessment of vascular patency was utilized in two cases.

Description of Individual Cases

SPT-1 a 37 year old black male with insulin dependent diabetes for 15 years had significant macrovascular changes and moderate diabetic retinopathy. He had an amputation of several toes in February 1980. On 3/3/80, he received a segmental cadaver pancreatic transplant with no HLA antigen matches. The pancreas was obtained from a 57 year old donor who had 30 minutes of warm ischemia. The pancreas was preserved under hypothermic pulsatile perfusion with albumin and plasmanate for 13 hours prior to transplantation. The pancreas never demonstrated any evidence of function after transplantation and had to be removed two days thereafter because of ischemic and infarcted pancreas. The cause of failure was due to perfusion and irreversible ischemic injury. There were no technical complications noted. Macroscopically, the tissue represented a soft mass weighing 77 grams with a homogenous dark brown

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surface. Microscopically, the specimen showed non-viable tissue with ischemic or coagulative necrosis involving the entire sample. A few inflammatory cells were seen along the periphery of the specimen (Figure 1). This patient is alive and on insulin coverage, 20 units of lente and 10 units of regular in the morning, and 5 units of lente and 5 units of regular insulin in the afternoon.

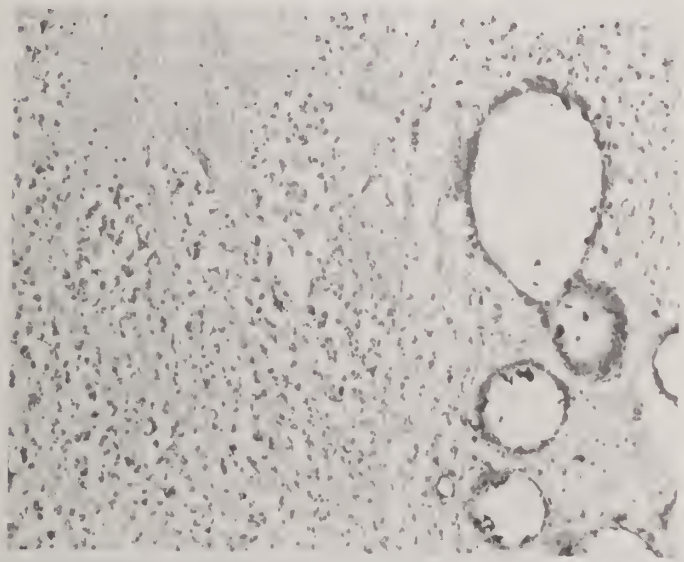

Figure 1. (SPT-1) The pancreas is completely infarcted and dead (HEx400).

SPT-2 a 20 year old black female with insulin dependent diabetes mellitus of ten years duration was difficult to control and had multiple episodes of ketoacidosis and coma. She also ahd moderate to severe diabetic retinopathy and hyperlipidemia. On 6/12/80 she received a segmental cadaver pancreas transplant with no HLA antigen matches and no evidence of warm ischemia during harvesting. The pancreas was transplanted two hours after removal from the donor, and during this time, it was kept under hypothermic storage (4°C) with Collins-albumin solution. After transplantation, the patient immediately became normoglycemic and remained that way for two months. A sudden rise in her blood sugar prompted biopsy of the specimen to rule out rejection. Microscopically, at this time the pancreatic tissue revealed some fibrous tissue with infiltration by polymorphonuclear leukocytes, lymphocytes, and plasma cells; arteritis and partially preserved islet cells, consistent with chronic rejection (Figure 2). In spite of antirejection treatment with ALG for 14 days, no response was noted. Therefore, the pancreas was removed 75 days after transplantation, and the patient required insulin coverage. The patient is alive and on insulin coverage. Grossly, the rejected pancreas was foul smelling and on cut section revealed a homogenous dark meaty surface. Microscopically, the pancreatic tissue revealed hemorrhagic necrosis with no viable tissue. A thrombus was noted occluding the lumen of a vessel, which already showed wevere subintimal hyperplasia and medial hypertrophy (Figures 3 and 4). It was felt that the thrombus was a terminal event associated with a progressive decreased in function of the pancreas, ultimately due to severe rejection and pancreatitis. Technical factors were ruled out as potential source of failure, after evaluating the laboratory and operative data of this case.

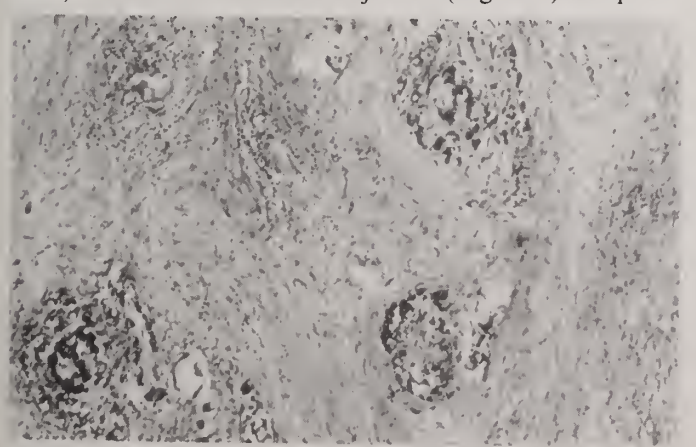

Figure 2. (SPT-2) Biopsy of a segmental pancreatic graft 60 days after transplantation reveals arteritis, fibrosis, infiltration by lymphocytes, plasma cells and few polymorphonuclear cells. PMNS; Few partiaily preserved islet cells are seen (HEx400).

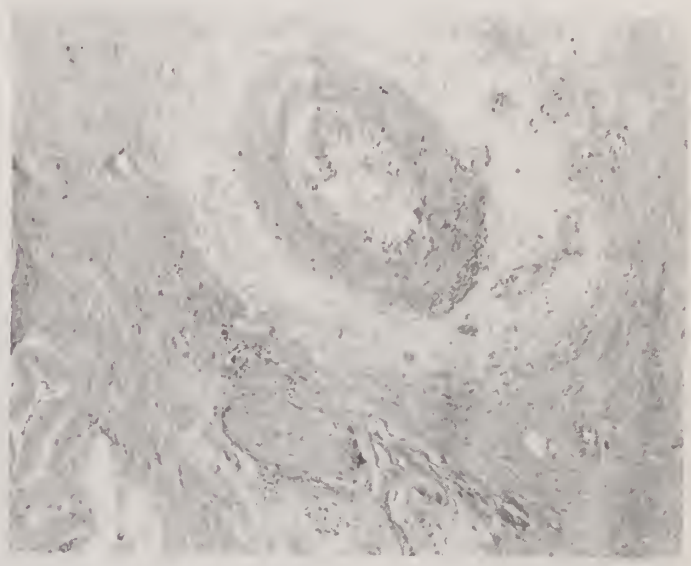

Figure 3. (SPT-2) The same case in Figure 2, 75 days after transplantation, with clinical evidence of rejection. A large artery showing severe subintimal hyperplasia with critical narrowing of its lumen. A large vein is also showing occlusion with recent thrombus (HEx400).

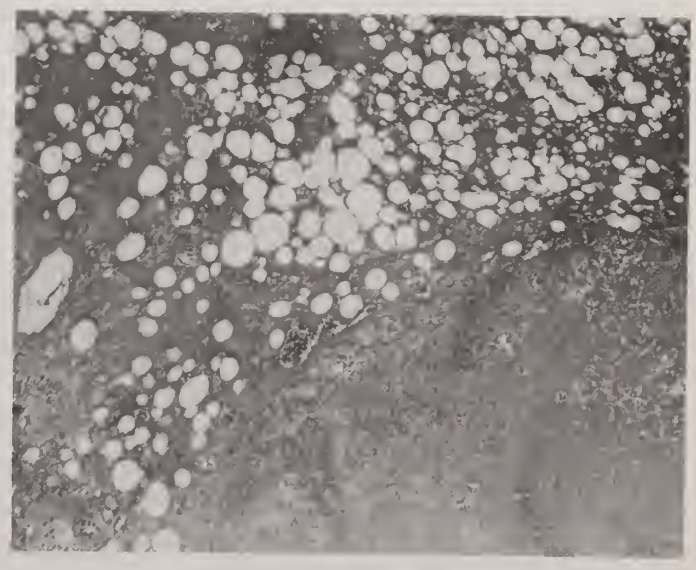

Figure 4 (SPT-2) Another area of the same case seen in Figure 3 showing infarcted and dead pancreatic tissue, 75 days after segmental pancreatic transplantation.

SPT-3 a 28 year old white male with insulin dependent diabetes mellitus since 14 years of age, was difficult to control with divided doses of lente inslin and had two hypoglycemic comas within the last year. He demonstrated moderate to severe retinopathy. On 7/9/80, he received a cadaver pancreatic transplant with no HLA antigen matches. There was no warm ischemia during harvesting. The pancreas was stored in Collins-albumin solution at 4°C for four hours prior to transplantation. Within two days after grafting in the post-operative period, the patient's plasma glucose levels dropped to within normal limits. He never received insulin post-operatively. Because of a sudden plasma glucose elevation on the 36th post-operative day, he received antirejection treatment with ALG for 14 days. On the 48th day, the pancreatic transplant was removed because of lack of response to the antirejection tratment. The patient is alive and on insulin coverage. Grossly, the pancreas was foul smelling and brown colored. On cut, the surface was smooth and hemorrhagic. Microscopically, non-viable necrotic tissue with inflammatory exudate at the periphery was noted. Vascular occlusion with thrombi was also noted. No bacterial colonies were noted. Again, in this case a similar conclusion as Case 2 was reached after carefully clinicopathological evaluation.

SPT-4 was a 30 year old black male with insulin dependent diabetes mellitus for 17 years and secondary retinopathy. He has previously had a left below knee amputation. Prior to his transplant, he was on regular insulin coverage of 45 units of lente insulin in the morning and 15 units in the evening. He received a segmental pancreatic transplant on 7/11/80 with no HLA antigen matches and no warm ischemia. The pancreas was stored in Collins-albumin solution at 4°C for four hours. Inmediately, in the post-operative period, his plasma glucose level dropped to within normal range. In the first few days post-transplant, he received a total of 500 rads of Cobalt 60 tele therapy to the transplant because of increased peripancreatic drainage. On 9/7/80, his blood sugar levels increased suddenly, and he was placed back on regular insulin. On 9/10/80, his transplanted pancreas was removed because of complete rejection. By this time, there was a total pancreas survival time of 61 days. He is alive and on insulin coverage. Grossly, the pancreatic tissue revealed small petechial hemorrhages with yellow granular areas. The cut section showed lobulated tissue with yellowish white areas. Microscopically, the pancreas showed infiltrates of small lymphocytes with plasma cells, interstitial fibrosis and subintimal hyperplasia with critical narrowing of its lumen. All these findings were consistent with chronic rejection.

SPT-5 was a 33 year old white female with insulin dependent diabetes mellitus since 17 years of age. She had several ketoacidotic episodes and multiple hypoglycemic reactions. She was taking lente insulin 26 units and 6 units of regular insulin daily. She had moderate to severe retinal changes and hypertension. On 7/24/80, she received a segmental pancreatic transplant with no HLA antigen matches. The harvested pancreas had no warm ischemia. It was stored under hypothermic storage with Collins-albumin solution at 4°C for six hours. In the first two days post-operatively, she was noted to have plasma glucose levels within normal limits. They remained normal for 46 days at which time there was an increase in the plasma glucose levels. The transplant was re-explored, and the organ removed because of rejection. This patient is alive and on insulin coverage. Gross and microscopic examinations of the transplanted pancreas showed evidence of rejection, with interstitial fibrosis and subintimal hyperplasia with vascular occlusion.

Discussion

The transplanted pancreases showed pathological changes compatible with chronic rejection and/or chronic pancreatitis, depending upon the time interval when the specimens were examined. In general, chronic rejection appeared first, and it was somewhat more consistently identifiable than chronic pancreatitis. The latter pathological diagnosis was recognizable always in association with chronic rejection. On the other hand, in the early stages after transplantation, chronic rejection was identified alone without evidence of chronic pancreatitis. The histological findings in these cases were very similar to what we usually see in the renal biopsies of clinically suspected chronic rejection of renal transplants. In the late periods of transplantation (>4 weeks), however, pathological findings of rejection were combined with chronic pancreatitis.

All completely rejected pancreatic transplants when removed revealed necrotic non-viable tissue. On careful examination in every case, large or medium sized arteries with marked subintimal hyperplasia resulting in narrowing of the lumen were found. Either a recent or an organized thrombus was noted occluding the lumen of such compromised blood vessels. All these changes were interpreted as consistent with pathological rejection rather than chronic pancreatitis. Especially, such vascular changes were rarely seen in chronic pancreatitis.

The differential diagnosis of chronic rejection and chronic pancreatitis was most difficult, as far as the microscopic pattern was concerned. The histologic picture of interstitial and lobular fibrosis with round cell infiltration in which small lymphocytes predominate along with partially destroyed or atrophied acinar cells and few viable islets of Langerhans in the absence of any clinical or laboratory information could easily be interpreted as chronic pancreatitis. Pathological and clinical features, possibly against the diagnosis of chronic pancreatitis were the following: 1) abnormal vascular findings of subintimal hyperplasia with narrowing of the lumen, and 2) consistently normal pancreatic function tests during the period of viable transplantation. An ongoing process of smoldering chronic pancreatitis during that period should have surely reflected some sort of abnormality in the pancreatic function tests.

Even though segmental pancreatic transplantation with duct occlusion with synthetic polymers has substituted pancreaticoduodenal transplants in the last few years,[12] [13] the occurrence of clinic pancreatitis following the injection of cyanoacrylate in our cases, casts some doubts as to the best available transplant method. More studies in this area are required to identify potential ways of preventing the appearance of chronic pancreatitis in the transplanted pancreas grafts.

In summary, the pathological findings of five human ductal occluded segmental pancreatic allografts removed at various intervals after transplantation are discussed in this work. Chronic rejection and pancreatitis were the main findings seen in this group of pancreases. Arterial and venous thrombosis, interlobular and perilobular fat necrosis, interlobular and perilobular fibrosis with round cell infiltration, and intimal thickening were common findings. Acute and chronic

inflammatory cells were noted in all the specimens obtained several weeks post-transplantation. The differential diagnosis of rejection and chronic pancreatitis was dificult without the clinical history. Rejection changes were present in all specimens, and chronic pancreatitis was associated with rejection only in the specimens, obtained several weeks (more than four) after transplantation. The study of these pathological specimens offer some help in the better understanding of acute and chronic changes occuring after ductal occluded segmental pancreatic transplantation. Advances in the recognition and management of early rejection, better long-term immunosuppression and modifications in the current surgical techniques would allow for better pancreas transplant survival.

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Epidemilogía de Infecciones del Tracto Urinario en Pacientes que Utilizan los Servicios de Medicina de Familia: Estudio Descriptivo

Rafael Iván Iriarte, MD, A.B.F.P.

Resumen: Se realiza un estudio de pacientes evaluados con sospecha de infecciones urinarias en una práctica de Medicina de Familia. Se describen los signos, síntomas y hallazgos de laboratorios que más correlacionan con cultivos positivos, la población más afectada y el patógeno más común.

En nuestra práctica diaria de Medicina de Familia, encontramos con frecuencia pacientes que presentan síntomas y signos sugestivos de infección del tracto urinario.

El instrumento que comunmente tenemos y con el cual contamos para ayudarnos rápidamente en nuestra impresión diagnótica, es el urinalisis simple o sedimiento urinario. Usualmente, para no retrasar el tratamiento, si los síntomas, signos y hallazgos de urinalisis nos sugieren que el diagnóstico es una infección del tracto urinario (ITU), solemos tomar un cultivo de orina y comenzar el tratamiento asumiendo que el agente etiológico más común es un coliforme gram negativo.

El presente es un estudio retrospectivo que pretende describir, en un período de seis meses, el o los patógenos más comunmente aislados por cultivo, su sensitividad a los agentes antimicrobianos, así como los síntomas y hallazgos de urinalisis más comunes en los pacientes con diagnóstico clínico de ITU.

Metodología

Se revisaron los expedientes de pacientes atendidos en Sala de Emergencia desde el mes de noviembre de 1979 hasta el mes de mayo de 1980. En la libreta de censo de estos expedientes, se encontraron un total de setenta y un (71) pacientes que tenían ITU como diagnóstico *provisional.*

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Al buscar las copias de estos expedientes hubo un total de 17 que por razones fuera de nuestro control no se encontraron. De los restantes 54 expedientes se obtuvieron 34 en los cuales se había descartado el diagnóstico de ITU en la misma visita y el diagnóstico final de Sala de Emergencia fue otro. Esto nos dejó con una muestra de 20 pacientes a los cuales se hizo un diagnóstico clínico de ITU en Sala de Emergencia, a base de historial, signos y hallazgos de urinalisis.

Los resultados de estos pacientes a base de sexo, edad, síntomas, sedimiento urinario y hallazgos de cultivo se detallan en la Tabla I.

Análisis e Interpretación de los Resultados

1. En 40% (8 de 20) de los casos que clínicamente se diagnosticaron como ITU se confirmó el diagnóstico con cultivo de orina positivo. (Se define como positivo aquel cultivo en que crecieron más de 105 colonias de un solo patógeno en muestras tomadas no cateterizadas. Cualquier crecimiento en orina cateterizada se considera positiva).
2. En la muestra general con diagnóstico clínico de ITU 75% de los pacientes eran de sexo feminino, 25% eran de sexo masculino.
3. De las pacientes de sexo femenino 60% (9 de 15) tenían entre 16 y 40 años de edad, 13% (2 de 15) tenían máas de 40 años y 27% (4 de 15) tenían edad pediátrica.
4. Los pacientes de sexo masculino tenían todos edad pediátrica o más de 70 años de edad.
5. De los pacientes de edad no pediátrica 48% presentaron como queja principal disuria, 31% presentaron con dolor suprapúbico y 23% con frecuencia.
6. Los pacientes de edad pediátrica, no presentaron ninguna tendencia marcada con respecto a síntomas de presentación, se presentaban igual, con disuria, fiebre y/o síntomas gastrointestinales.
7. En un 45% de los casos se utilizó Ampicillin como medicamento de elección, en un 45% se utilizó Trimetropin/Sulfametoxazole y en el restante 10% se usó Cefalotina.
8. De los casos confirmados con cultivos 63% (5 de 8) fueron mujeres entre 16 y 40 años, 25% (2 de 8) fueron mujeres de más de 40 años y 12% (un caso) se trató de un hombre de más de 70 años.
9. De los 8 pacientes que tuvieron cultivos positivos, 6 (75%) tuvieron como agente etiológico el organismo Escherichia Coli. El agente patológico de los otros dos casos (25%) fue un Staphilococus.
10. Todos los organismos cultivados, con excepción de 1 caso de E. Coli, eran sensitivos a Ampicilina, Trimetropim/Sulfametoxazole, Cefalotina, Acido Nalidixico y Nitrofurantorina, que son los agentes antimicrobianos

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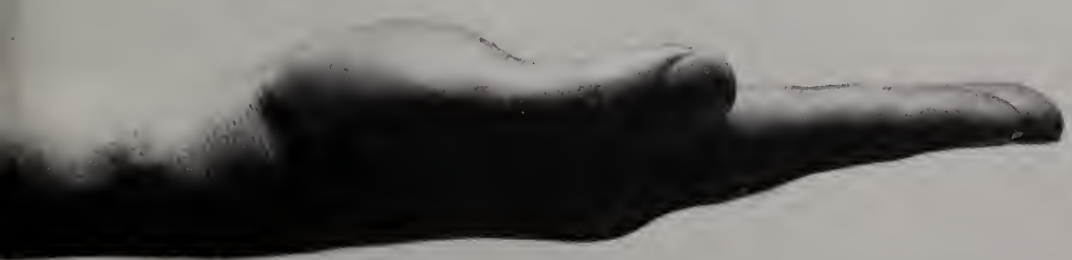

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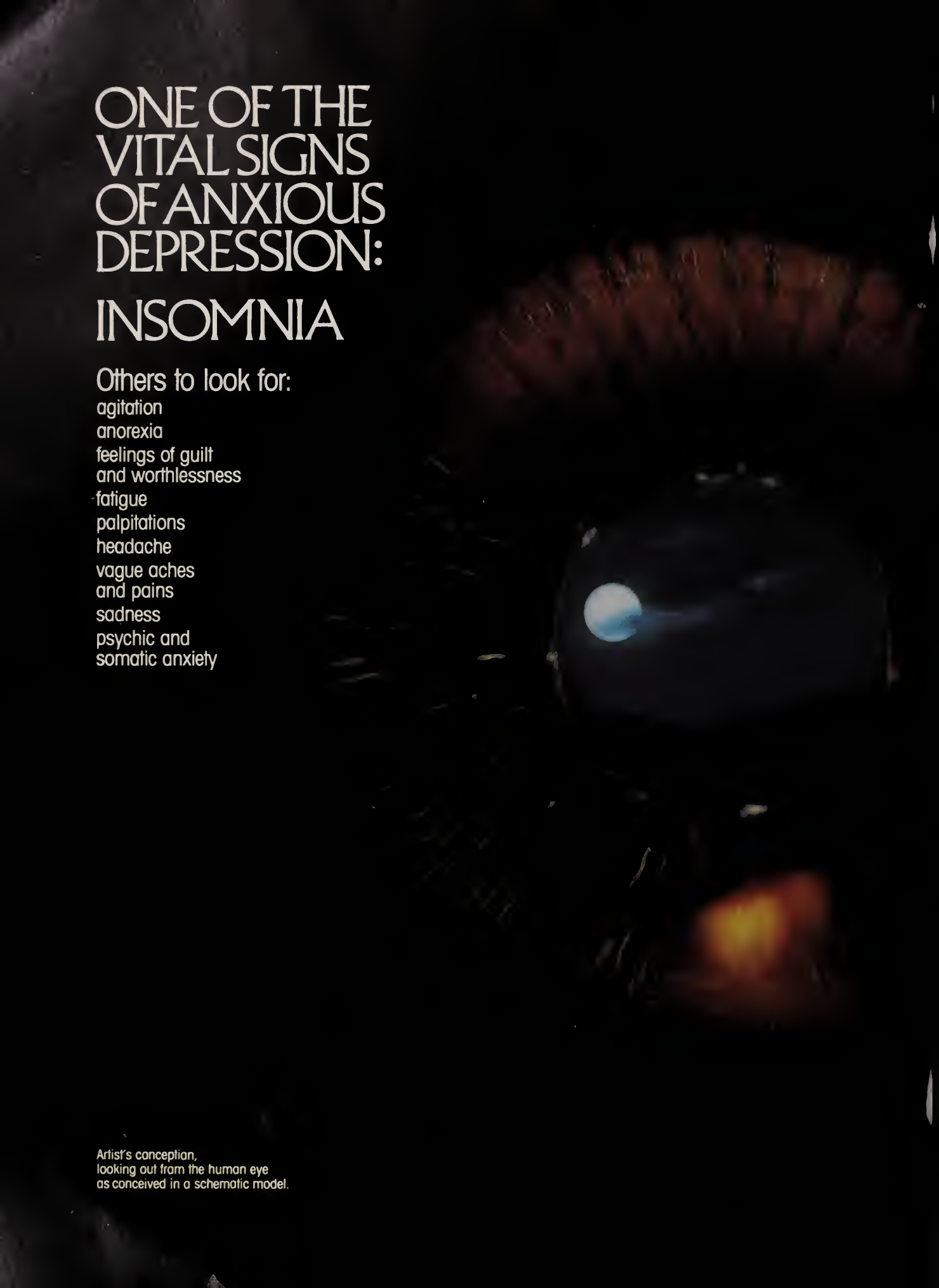
feelings of guilt and worthlessness
fatigue
palpitations
headache
vague aches and pains
sadness
psychic and somatic anxiety



Artist's conception,
looking out from the human eye
as conceived in a schematic model.

ROCHE

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TABLA I

Resultados: Diagnóstico Clínico ITU en Sala de Emergencia

Pcte.	Sexo	Edad	Síntoma Principal	Sedimento Urinario			Tratamiento	Cultivo
				WBC	BACT	RBC		
1	F	16	disuria	—	alguno	muchas	Ampi	EColi 105
2	F	44	disuria	mucha	mucha	—	Ampi	EColi 105
3	E	47	frecuencia	mucha	occ	—	T/STX	EColi 105
4	E	8	disuria	30-40	alguna	—	Ampi	EColi 105
5	F	24	disuria	22-25	muchas	—	T/STX	EColi 105
6	F	37	disuria	mucha	alguna	—	Ampi	Staph 105
7	M	5mo	fiebre, diarrea	mucha	mucha	—	Ampi	EColi 26,000
**8	M	86	disuria	no se encontró U/A			T/STX	EColi
9	F	23	dolor suprapúbico	(cath)	occ	—	Ampi	O col
10	E	4mo	fiebre	7-10	occ	—	Ampi	no resul.
11	F	8	disuria	40-50	muchas	—	T/STX	EColi 18,400
12	F	25	frecuencia	muchas	mod.	—	T/STX	EColi 105
13	E	33	disuria	50	muchas	—	Cefalotin	Staph 105
14	M	3	hipoactividad	6-8	occ	—	Ampi	no se tomó
15	F	21	dolor suprapúbico	3-5	algunos	—	T/STX	no se tomó
16	M	72	frecuencia	5-8	muchas	—	T/STX	3 organi.
17	E	16	dolor suprapúbico	1-5	muchas	—	T/STX	O col
18	F	3	disuria	0-3	muchas	—	Cefalotin	no se tomó
19	F	32	dolor suprapúbico	14-16	algunas	—	T/STX	no se tomó
20	M	5mo	fiebre	6-3	occ	—	Ampi	O Col

Ampi = Ampicillin T/STX = Trimetropim/Sulfametoxazole
WBC = Células blancas RBC = células rojas
**Todos los patógenos aislados fueron sensibles en vitro a Ampicillin, T/STX y Cefalothin excepto el del caso núm. 8 que era sensitivo solo a Gentamicina.

usualmente usados empíricamente para ITU.

11. De los 8 casos de cultivos positivos, en 6 (75%) se habían encontrado más de 20 células blancas por campo microscópico.
12. De los 12 casos de cultivos negativos, solamente en 3 (25%) habían más de 20 células blancas por campo. En los tres cultivos de estos casos crecieron E. Coli entre 18,000 y 35,000 colonias.

En los cultivos de orina que presentaban menos de 20 células blancas por campo no hubo crecimiento de patógenos. Hubo un caso que presentó 14-16 células blancas en el cual no se tomó cultivo. Este análisis se vio afectado por el dato de que en algunos casos no hay evidencia de que se tomara cultivo o no se encontraron los resultados del mismo.

Conclusión

El paciente que más comunmente vimos con diagnóstico de infección de tracto urinario es una mujer entre 16 y 40 años de edad que se presenta con síntoma de disuria o dolor suprapúbico.

Debemos estar atentos en pacientes de edad pediátrica que pueden presentar con ITU y síntomas y signos no específicos.

El patógeno más común en la población estudiada es un Escherichia Coli sensitivo a Ampicilina y a Trimetopina /Sulfametoxazol que son los agentes más comunmente utilizados empíricamente para tratar ITU. El hallazgo de urinalisis que parece correlacionar más con el crecimiento de bacterias en cultivo es el de piuria marcada de más de 20 células por campo.

Los hallazgos de este estudio parecen correlacionar con los de Wilks[1] quien en 1979 describió en un estudio que el 100% de los pacientes con cultivo con más de 10^5 colonias tenían piuria signficativa (75/campo) en el sedimento urinario. Un 18% de los pacientes con cultivos positivos (10^5 col) no tenían bacteriuria como hallazgo de urinalisis. En ese mismo estudio 17 de 50 pacientes que tenían piuria tuvieron cultivos negativos. El autor concluye que el hallazgo de aumento en células blancas en el sedimiento urinario es sensitivo pero *no* específico para el diagnóstico de ITU. Por el contrario Bonadio[2] en el 1979 encontró en su estudio que el hallazgo de urinalisis que más correlacionaba con cultivos positivos fue el de bacteriuria. Sin embargo este último autor utilizó como metodología la microscopía de orina *no* centrifugada. Esta diferencia en técnica puede explicar los hallazgos diferentes.

En resumen, se ha intentado describir un perfil del paciente típico visto en el programa de Medicina de Familia del Hospital Regional de Caguas con diagnóstico de ITU. Se han descrito también los síntomas, signos y hallazgos de laboratorio que más correlacionan con bacteriologías positivas.

El patógeno más importante que causa ITU en nuestro medio ambiente parece ser un E. Coli susceptible a la mayoría de los agentes terapeúticos más usado empíricamente.

Abstract: A descriptive study of patients seen in a family practice with suspected urinary tract infection. It correlates the frequency of presenting signs, symptom, and urinary microscopy findings with positive cultives. The population at risk and the most prevalent pathogen found in the cultives is also described.

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P·I·A

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Chronic Non-Specific Diarrhea of Infancy

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Summary: Chronic non-specific diarrhea (CNSD) is the most common form of prolonged or recurrent diarrhea in infants and toddlers. It usually begins shortly after weaning or as a post-infectious diarrhea. The mechanism of diarrhea is probably via a multiple protein intolerance, with antigen penetration occurring "physiologically" in the newborn period or secondary to mucosal damage later in infancy. The course of CNSD is characterized by cycles of loose stools, usually accompanied by some atopic symptoms. The diarrhea persists in spite of multiple formula changes, but the child usually gains weight normally. Problems arise when the diet is adversely manipulated to prevent normal caloric intake or when gastroesophageal reflux is severe. "Gut rest" and parenteral alimentation may be necessary in the latter. Otherwise, management consists of using only one formula in spite of the diarrhea, avoiding elimination diets, assuring a good caloric intake and corresponding weight gain, and a varied table food diet for toodlers. The diarrhea will resolve spontaneously and not recur after age three.

The most common form of chronic or recurrent diarrhea among infants and toddlers in the continental U.S. and in Puerto Rico has several distinguishing features: 1) no infectious etiology can be found, 2) no serious underlying intestinal disease is present, 3) the diarrhea persists despite multiple formula changes, 4) typically there is adequate weight gain, and 5) the diarrhea stops spontaneously sometime before the third birthday.

There has been no consistent terminology applied in the literature to a chronic diarrhea of infancy which fulfills the above criteria. Terms such as milk allergy, milk intolerance, post-infectious diarrhea and chronic benign recurrent diarrhea probably reflected the suspicion that different disease mechanisms were behind the somewhat different clinical pictures being reported. Based on recent experimental and clinical observations, we believe that these conditions may now be grouped under one broad heading-chronic non-specific diarrhea (CNSD). In this short review, we will state the case for considering all degrees of CNSD as products of one pathogenetic mechanism —multiple protein intolerance, and then detail our approach to and management of this all-too-common problem. Hopefully, the primary care physician will then find dealing with these patients a more sensible and productive endeavor.

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Pathogenesis

A number of forms of severe damage to the gastrointestinal tract have been positively correlated to the consumption of soy and cow's milk protein. Halpin et al[1] describe a group of infants who presented with vomiting, diarrhea, hematochezia and weight loss after a trial of soy protein formula. Rectal biopsy performed within 24 hours of the challenge showed an acute colitis with crypt abscesses, findings which precluded distinguishing these cases histologically from infectious or mild ulcerative colitis. Ament and Rubin[2] reported a six week old infant who, within 24 hours of an exposure to soy protein, developed fever, leukocytosis, cyanosis, vomiting, massive blood-tinged mucoid diarrhea, dehydration, metabolic acidosis and a flat jejunal mucosa on biopsy. Waldman et al[3] presented six patients with a syndrome characterized by edema, growth retardation, extreme hypoalbuminemia, anemia, and peripheral blood and intestinal mucosal eosinophilia. They subsequently documented that a protein-losing exteropathy existed secondary to cow's milk ingestion.

Atopic reactions not involving the gastrointestinal tract have also been reported for some time in association with consumption of various types of milk. While dermatitis[4] and asthma[5] may be the more common manifestations, it should be appreciated that at least one infant who had previously exhibited vomiting, asthma and a rash while on a soy protein-based formula, was documented to go into anaphylactic shock when inadvertently given the same formula at the age of 20 months[6].

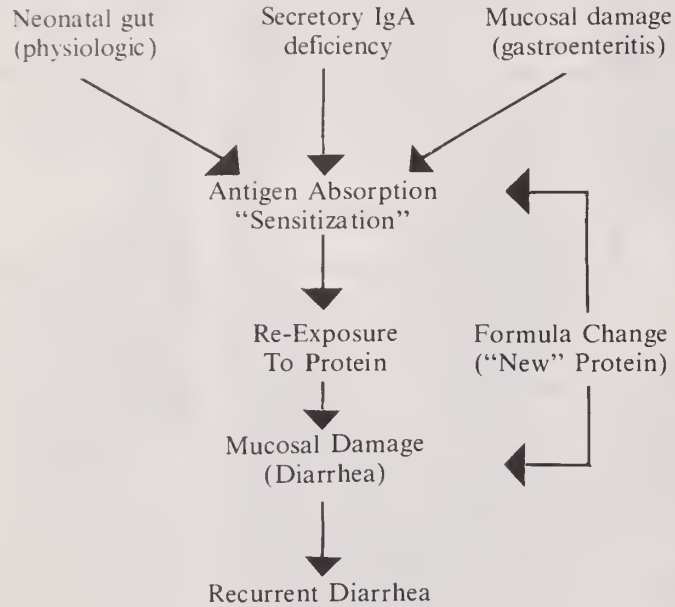
These observations are important in two ways. First, they demonstrate the ability of milk proteins to act as antigens capable of causing significant intestinal mucosal destruction by presumed immunologic phenomena. Second, they demonstrate that milk antigens may find their way into the systemic circulation and induce peripheral immunologic-type reactions without appreciable damage occuring at the intestinal múcosal level.

Intact macromolecules have been documented to penetrate the neonatal gut in sufficient quantity to induce a specific systemic antibody response[7 8 9]. During or shortly after weaning, "closure" occurs and the gut becomes impermeable to macromolecules unless special circumstances supervene. Disruptions of the intestinal mucosal surface barrier, as during acute gastroenteritis[10] or in the case of secrtory IgA deficiency[11], facilitate the entry of dietary protein

antigens. The excess antigen load at these times may be the initial "sensitizing" event, or in an infant "sensitized" during the first weeks of life, this reexposure may culminate in additional mucosal damage (Figure 1).

FIGURE I

Proposed Mechanism of CNSD



In view of the observations that milk proteins can produce a gamut of local and systemic disease, and that the mechanism probably involves a re-exposure to a "sensitized" gut, we postulate that the clinical syndrome of CNSD can be understood as occupying a place in the spectrum of dietary protein intolerance (Table I) where there is enough "damage" to produce diarrhea, but not enough to compromise physiologic caloric absorption. Just what the intestinal mucosal "damage" consists of in CNSD is not clear. While a significant number of patients with a post-infection-type diarrhea will have an enteropathy with partial villous atrophy[15], most patients will show a normal small intestinal biopsy[16]. Lack of a histologically demonstrable lesion does not, however, rule out macromolecular penetration by cell-surface phenomena. This is presently an area of intense medical research.[17] What may begin as an intolerance to only one dietary protein may shortly escalate into a multiple protein intolerance as new protein sources (formulas) are fed to a still damaged bowel, a setup for penetration and "sensitization". In this regard, Powell[18] has observed that soy protein intolerance is more likely to develop when soy protein formula is introduced too soon after a gut has been damaged by a cow's milk allergy reaction. It is typical to have a new formula introduced during a particularly "bad" spell of diarrhea. At this point, in CNSD, transient improvement is followed by a return of equally loose stools and the cycle is then repeated as parents and doctor exhaust all known formulas.

TABLE I

Spectrum of Dietary Protein Intolerance
Anaphylaxis
Ulcerative Colitis-like Syndrome
Necrotizing Enterocolitis-like Syndrome[12]
Protein Losing Enteropathy
Gastrointestinal Blood Loss[13]
Flat Intestinal Mucosa
Carbohydrate Intolerance[14]
Chronic Non-Specific Diarrhea
Gastroesophageal Reflux
Atopic Symptons

Diagnosis and Management

CNSD usually has its onset between two and six months of age, often shortly after breast feeding has been abandoned. It is not uncommon, though, to see CNSD begin between the first and second year of life. It's duration varies considerably, lasting from a couple months to a couple of years, yet all cases are "outgrown" before the age of three.

There are two typical case histories, In one, the mother has recently discontinued breast feeding, and the infant is on a cow's milk formula. For no apparent reason, the child may begin with diarrhea, vomiting, spitting up and/or "colic". No infectious agent can be identified, the formula is changed and transient improvement gives way to renewed "intolerance". The other typical case involves a healthy infant who had previously tolerated formula feedings well. He or she contracts an infectious gastroenteritis whose course runs the expected two to three days. After the initial diarrhea has subsided, however, and the infant is restarted on his old formula, there is a relapse of vomiting and/or diarrhea, sometimes substantial enough to call for rehospitalization (what we commonly refer to in P.R. as "un rebote"). The infant's formula is then changed, usually to a soy-based product, trying to avoid a lactose-containing milk. Transient improvement is followed within a week by renewed diarrhea and the magic formula chase is on again.

The severity of the reaction to the milk product will be seen to vary significantly (Table II). While one child may only exhibit bouts of loose watery stools, another may have accompanying atopic manifestations such as asthma, rhinorhea, middle ear effusions or dermatitis. A characteristic

TABLE II

Clinical Spectrum of CNSD
Failure To Thrive
Gastroesophageal Reflux
Chronic Recurrent Diarrhea
Recurrent Middle Ear Disease[19]
Other Atopic Symptoms

of CNSD is that both the diarrhea and the atopic manifestations tend to run together in cycles, the infant or young child being relatively symptom free for up to several weeks at a time, even though the diet is not being altered.

In general, the clinical course of the disease represents more of a strain on mother's patience than anything else, since she has to tolerate the nuisance of multiple diaper changes and not having a child toilet-trained as quickly as she had hoped. Since these patients lack a malabsorption problem, they continue to gain weight and grow normally if their diet is handled properly.

Infants with CNSD may present, however, with failure to thrive. This is a common occurrence[20] and is usually secondary to prolonged dietary manipulations resulting in a hypocaloric diet being consumed over a number of weeks or months. As we have alluded to, parents, many times with the help of their pediatrician, see fit to treat each cycle of "bad" diarrhea with clear fluids and a number of days of partial strength formula supplemented with juices and/or electrolyte solutions. In addition, a number of foods are eliminated from the diet in the belief that the child is allergic or intolerant to them. Since the "bad" diarrhea may recur every week, the end result within months is a malnourished child secondary to an inadequate caloric intake.

The management of this situation, once recognized, is simple. CNSD, representing a multiple protein intolerance, can be anticipated to cause loose stools regardless of the formula used. However, CNSD implies that there is no malabsorption present, so the infant should grow normally if only he is given enough calories. The solution, then, is to deemphasize the diarrhea in the parent's eyes, and insist that the infant be placed on just one formula (whichever has best been tolerated in the past), that it be given full strength, and that a regular, varied, balanced diet for age be otherwise maintained.

A more difficult problem to manage is the infant with CNSD who develops an allergic gastropathy; with significant vomiting and/or gastroesophageal reflux. This may lead to an inability to feed the child orally and on occasions parenteral alimentation and "gut rest" are the only alternative. Upper GI series performed on these patients typically reveals antral spasm and delayed gastric emptying and the radiologist may interpret the study as suggestive of peptic ulcer disease. Endoscopy may show antritis and possible duodenitis, Although these particular cases may require a week or two of "gut rest", at the end of this period the same formula may be re-introduced and reasonable tolerance anticipated. Thus, we still consider these patients as falling within the clinical spectrum of CNSD.

The recognition that these infants with gastroesophageal reflux are exhibiting phenomena related to a transient protein intolerance is of cardinal importance, since the reflux problem may be assessed to be serious enough, by some, to warrant a fundoplication. Two findings should direct one's attention away from surgery as a solution. First, in any infant with chronic recurrent diarrhea, significant gastroesophageal reflux is most likely secondary to protein intolerance. Second, an acid reflux test which shows a Type II pattern, as described by Jolley and co-workers[21], suggests antralpylorospasm, and protein intolerance may be the cause. In any of these situations, parenteral alimentation with "gut rest" followed by trials with protein hydrolysate formulas should be diligently pursued in order to maintain weight gain and avoid surgery for a condition which will shortly be "outgrown".

Before closing with a summary of the important aspects of management, we must emphasize that CNSD still remains a diagnosis of exclusion and that a few conditions must always be considered and ruled out when dealing with an infant or young child with chronic diarrhea, before ascribing all problems to protein intolerance.

Fat malabsorption syndromes should be ruled out if adequate weight gain does not ensue while on "growth" calories. Lactose intolerance can easily be ruled out by changing formulas or by performing a lactose tolerance test. The cyclic nature of diarrhea secondary to chronic giardiasis may be confused with CNSD, so should there be a strong clinical suspicion, various diagnostic modalities should be attempted in an effort to isolate the organism. In general, though, an infant with chronic diarrhea on multiple formulas, who is gaining weight and in whom giardiasis has been ruled out, probably has CNSD.

The management of these infants has already been alluded to in discussing the clinical presentation but we would like to re-emphasize certain principles. The physician and parents need to be guided by the realization that: 1) these infants have the capacity to react with diarrhea to any type of formula, 2) there is no serious underlying bowel disease and therefore, the ability to grow and gain weight will not be affected as long as an adequate amount of calories are given daily, and 3) the condition will resolve spontaneously.

In practical terms, this means that: 1) The parents and physician should settle on the one formula which has produced the least amount of problems and is well accepted by the infant. The parents must persist in giving that formula to their child even though it means cycles of loose stools. As long as the child gains weight, the diarrhea is medically inconsequential; 2) For the older infant, solid foods may be started on schedule and the toddler should be encouraged to eat a varied balanced diet of "table food"; 3) Oral electrolyte solutions and partial strength formulas should be used as infrequently as possible and only when the intolerance (vomiting or diarrhea) is marked. The emphasis toward the parents should be that the child needs calories and that full-strength milk, even if it produces loose stools, is by far the best source of calories until a full "table food" diet is accepted.

For the young infant on an exclusive formula diet, one may consider the use of protein hydrolysate formulas (Nutramigen, Pregestimil). There is theoretical and experimental evidence[22] to suggest that the hydrolyzed protein fractions are not as antigenic as cow or soy protein formulas, and for this reason, one or the other or both may be tried, especially in an infant in whom reflux is a significant problem. Reason dictates that these formulas be introduced at a quiescent period in the diarrhea cycles or after a couple of days of "gut rest" to minimize penetration and subsequent sensitization. We all too frequently see, however, that these formulas have already been tried and abandoned because they offered no improvement.

Lastly, there has been some recent advocacy of a high-fat diet to treat CNSD[23 24]. The reasons for it's sometimes dramatic alleviation of the diarrhea is by no means clear. We have had varied success using it, and since it appears harmless, it is probably worth a try in the toddler age group.

Resumen: La diarrea crónica no específica (DCNE) es la forma más común de diarrea prolongada o recurrente en infantes. Usualmente comienza poco después del destete o como una diarrea post-infecciosa. El mecanismo de la diarrea es probablemente vía una intolerancia múltiple a proteínas, con la penetración antigénica ocurriendo "fisiológicamente" en el período neonatal o secundario a un daño a la mucosa intestinal más tarde en la infancia. El curso clínico de la DCNE se caracteriza por ciclos de diarrea, usualmente acompañados por algunos síntomas atópicos. La diarrea persiste a pesar de cambios múltiples de fórmulas, pero el infante generalmente sigue ganando peso. Surgen problemas cuando la dieta es adversamente manipulada y prohibe se consuma cantidad suficiente de calorías o cuando el reflujo gastroesofágico es severo. Intestino en reposo y alimentación parenteral suelen ser necesarios en el último caso. De otra manera, el manejo consiste en ofrecer solo una fórmula, evitando dietas hipocalóricas. Al año, se debe ofrecer una dieta completa y variada. La DCNE desaparece espontáneamente antes de los tres años de edad.

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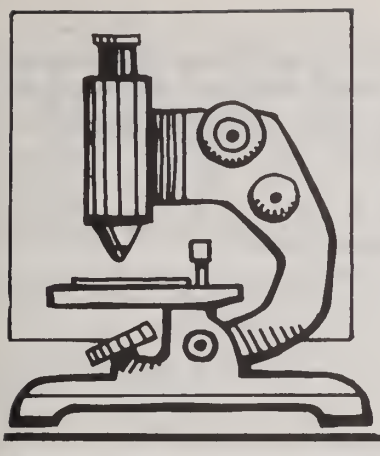

ARTICULOS DE INVESTIGACION

Nonspecifity of Elevated Serum Phosphate Levels in the Diagnosis of Intestinal Ischemia

Manuel E. Lores, MD
Luis A. Morales, MD
Pedro J. Roselló, MD, FACS

Abstract: **Significant elevation in serum phosphate levels is not specific of intestinal ischemia, also occuring in the experimental situation of bacterial peritonitis and of limb ischemia. In addition, to this, by the time the increase in serum phosphate becomes significant in intestinal ischemia, irreversible vascular changes and bowel gangrene are already present. These results argue against the use of this laboratory test as a specific parameter in the early diagnosis of intestinal ischemia.**

It has been recently reportd by Jamieson et al that increased inorganic phosphate levels both in serum and peritoneal fluid occur in early intestinal ischemia.[1,2] Based on their experimental work these authors suggested that this test could be useful in making an earlier diagnosis of intestinal infarction. However, using the same experimental model, we have found that the serum phosphate rose significantly only after loss of viability and bowel necrosis were established.[3]

The present experimental study was designed in an attempt to determine the "specificity" of increased serum phosphate levels in the diagnosis of intestinal ischemia.

Material & Methods

Thirty mongrel dogs were used. In group I, 10 dogs were submitted to massive intestinal ischemia by double ligation of the superior mesenteric artery at its origin from the abdominal aorta. In group II, 10 dogs were submitted to severe limb ischemia by proximal ligation of the right common iliac artery. In the remaining 10 dogs, group III, peritonitis was established according to the method described by Rosato.[4]

Serum phosphate levels were measured at 0.2,4,6,8,12,24 and 48 hours in groups I and II, and at 0,24 and 48 hours in group III.

All results were expressed as the mean ± one standard deviation. Statistical analysis was carried out using the Student's t-test. No significance was ascribed to a difference with a p value greater than 0.05.

TABLE I

Serum Phosphate Levels, In Three Experimental Groups (Milligrams Percent)

Group	(Time hrs.)							
	0	2	4	6	8	12	24	48
Intestinal Ischemia (I)	3.88±1.2	4.62±1.1	4.51±1	5.42±0.9**	5.37±0.7**	5.44±0.7**	5.58±1.5*	—
Limb Ischemia (II)	3.86±0.5	3.95±0.8	4.83±1*	5.14±1**	5.08±0.8**	5.14±0.8**	4.76±1*	4.94±1
Peritonitis (III)	4.26±1.2						4.55±1.1	6.08±2

Values are mean ± S.D. Each group compared to 0 hours by Student's t-test.
* $p < .05$
** $p < 0.01$

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Results

The serum phosphate levels rose significantly in each of the three experimental groups as compared with their own baseline values (table I). In the intestinal ischemia group the

rise in serum phosphate was significant and persistent after 6 hours of ischemia ($p<.01$). In the limb ischemia group it appeared after 4 hours ($p<.05$). Finally, in the peritonitis group the elevation in serum phosphate became significant after 48 hours of septic course ($p<.05$). (Figure 1).

There were no deaths in the limb ischemia or in the bacterial peritonitis groups at the end of the 48 hours period of the study. However, only 6 dogs in the intestinal ischemia group survived 24 hours (40% mortality) and none reached the 48 hours end point of the experiment (100% mortality).

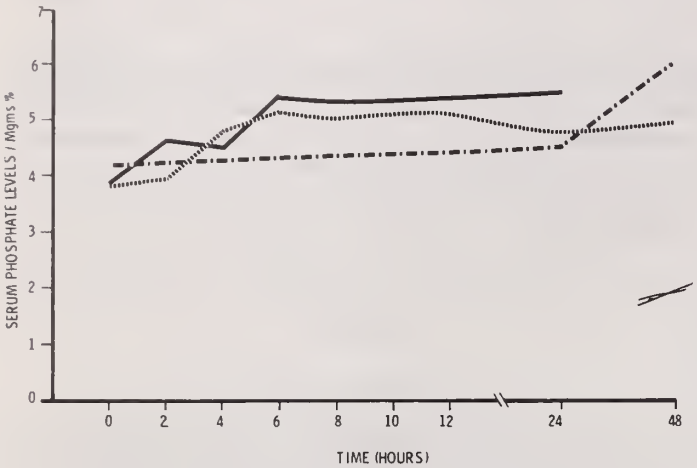

Figure 1. Serum phosphate levels, milligrams per cent, at different times among the three experimental groups: intestinal ischemia (solid line), limb ischemia (dotted line) and bacterial peritonitis (broken line).

Discussion

In accordance with our previous experimental work[3] it was again demonstrated that the elevation of serum phosphate in intestinal ischemia is a delayed phenomenon associated with irreversible ischemic changes, bowel gangrene, and a high mortality.

Our present data suggests that this elevation of serum phosphate is not specific of intestinal ischemia, occuring also in the experimental models of limb ischemia and bacterial peritonitis.

It seems reasonable to postulate that inorganic phosphate, the major intracellular anion, is liberated to the extracellular fluid with severe cell injury or death, and therefore is significantly increased in the serum after any such injury to an extensive cell mass. In our previous study.[3] We concluded that increased levels of serum phosphate in intestinal ischemia were associated with irreversible bowel necrosis precluding its use as an early diagnostic sign in this serious intraabdominal condition. From our present data we must add that this elevation in serum phosphate is not specific of intestinal ischemia, but occurs after any significant injury to a large cell mass.

Resumen: La elevación de los niveles séricos de fosfato no es específico de isquemia intestinal. También aparece experimentalmente al provocar peritonitis bacteriana y con isquemia de las extremidades. Además, cuando aparecen elevaciones significativas del fosfato sérico por isquemia intestinal ya han ocurrido cambios vasculares irreversibles y gangrena intestinal. Los resultados obtenidos experimentalmente constituyen un argumento de peso contra el uso de esta prueba de laboratorio (fosfatos séricos) como parámetro específico en el diagnóstico temprano de isquemia intestinal.

Acknowledgements

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PRESENTACION DE CASOS

Intermittent Atrio-Ventricular Block Related to a High Grade Stenosis of the Right Coronary Artery

Pablo I. Altieri, M.D.
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Efraín Defendini, M.D.

Abstract: **A patient with high grade stenosis of the right coronary artery presented with episodes of intermittent atrio-ventricular block requiring coronary bypass surgery to abolish these episodes.**

One on the causes of atrio-ventricular block is obstructive coronary disease. As a rule AV block as a sequela of myocardial infarction and the anatomic changes in the conduction system are irreversible, requiring the implantation of a permanent pacemaker. Rarely, A-V block may be caused by intermittent ischemia of the atrio-ventricular node. It is our purpose to present our experience with such a patient.

Case Report

P.R., a 49 year old premenopausal woman was admitted to another hospital complaining of recurrent chest pain. She did not give a history of coronary risk factors except for smoking. While in the coronary care unit she developed episodes of A-V block related to chest pain (Fig. 1). A temporary pacemaker was employed, but her symptoms persisted despite the use of nitroglycerin and propranolol.

The patient was transferred to the University Hospital for further evaluation. Physical examination was within normal limits except for an atrial gallop. Chest X-ray was normal as was the EKG except during episodes of chest pain, which showed the changes seen in Figure 1.

She underwent cardiac catheterization shortly after admission. The right and left heart pressures were normal. Left ventricular ejection fraction was calculated at 56%. Coronary angiography showed a dominant right coronary artery with two areas of 90% obstruction of the junction of right coronary artery with two areas of 90% obstruction of the middle and distal thirds of the vessel. (Fig. 2)

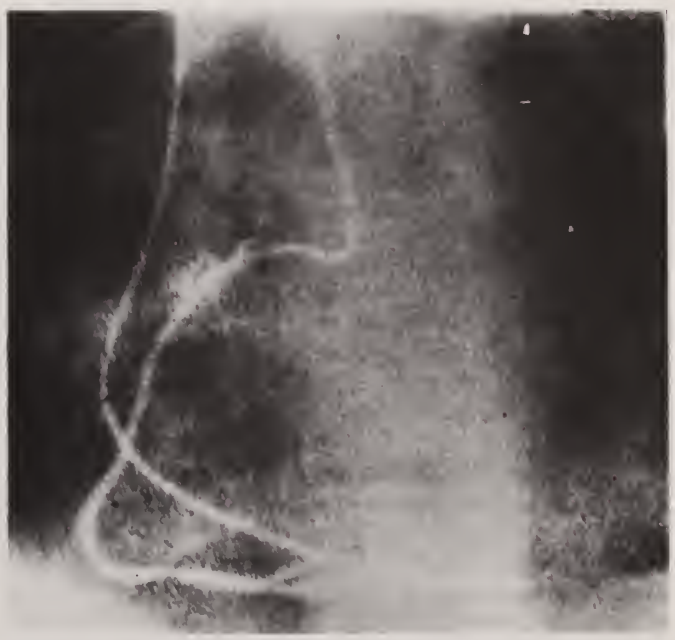

FIGURE 2
Right coronary arteriogram in the left anterior oblique position showing two 90% obstructive lesions.

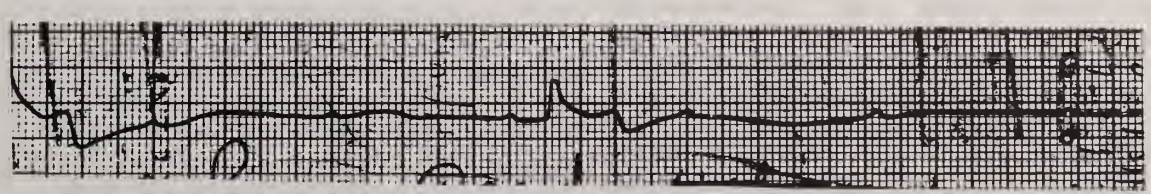

FIGURE 1 **Monitor strip showing complete atrio-ventricular block.**

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The left coronary artery was small and free of obstructive lesions. Atrial pacing showed a normal sino-atrial recovery time of 800 msec. and 1: atrioventricular capture up to 150 beats per minute. After catherization her symptoms persisted even with optimal medical management. She suffered cardiac arrest from which she was resuscitated. This, prompted the performance of a saphenous vein aorto coronary bypass graft to the right coronary artery. A permanent pacemaker was implanted at operation. The early postoperative period was characterized by repeated episodes of ventricular fibrillation, treated with electric shock and intravenous lidocaine. No intraoperative infarction was authenticated. The patient was discharged much improved and has remained asymtomatic returning to her normal activities.

Discussion

The role of spasm in the genesis of myocardial ischemia is under intensive study. Oliva[1] in 1973 demonstrated coronary arterial spasm to be the cause of severe, reversible myocardial ischemia in a patient with Prinzmetal angina. Others have confirmed that spasm of a normal or atherosclerotic coronary artery is the mechanism in most patients with Prinzmetal angina.[2] [3]. Oliva[4] described the importance of coronary arterial spasm in acute myocardial infarction. He reported 40% coronary arterial spasm in patients with acute myocardial infarction. He found that spasm always occurred at the site of an atherosclerotic obstruction. One of his patients with obstructive coronary disease in the right coronary artery was in complete heart block. After the use of intracoronary nitroglycerin the A-V block disappeared.

It has been hypothetized that spasm is secondary to other stimuli like increase catecholamines[5] acting on alpha adrenergic receptors, local hyperkalemia or vasoactive substances released from platelet aggregates. Platelet aggregates are present in the epicardial and intramyocardial arteries of patients who die suddenly due to obstructive coronary disease.[6] [7] The release from platelet aggregates of vasoactive substances such as serotonin, thromboxane[8] and prostaglandins may produce spasm. A transient sympathetic discharge related to cigarette smoking[9] or the rapid eye movement (REM) phase of sleep[10] has been shown to produce spasm.

In our case, we think that the patient was having intermittent spasm in the area of the right coronary artery producing intermittent ischemia of the atrio-ventricualr node and atrio-ventricular block. The normal sinus and atrio ventricular node function during atrial pacing tends to corroborate this observation.

After the coronary bypass surgery the patient has remained asymptomatic and in normal sinus rhythm. It was noticed that most of the episodes of chest pain and atrioventricular block occurred while the patient was sleeping probably related to the REM phase.

These observations point to the role of intermittent spasm superimposed on a fixed coronary obstruction, producing more ischemia of the conduction system and in this way conduction abnormalities.

Resumen: Un paciente con una obstrucción severa de la coronaria derecha se presentó con episodios intermitentes del bloqueo atrioventricular. Un puente arterio-coronario abolió estos episodios.

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ARTICULOS ESPECIALES

Ambulatory Surgery at Ponce Regional Hospital

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This study was carried out to evaluate the results of the ambulatory Surgery Program at Ponce Regional Hospital during a three year period (1977-1980). A total of 1,787 patients underwent surgical procedures using general anesthesia or local anesthesia supplemented by neurolepto-anesthesia, under supervision of an anesthesiologist during this period.

A brief description of the organization of the unit is given. Results are evaluated according to type of surgery carried out, the presence or absence of complications and the need for hospitalization.

The study demonstrated that patients received the same type of treatment usually given to hospitalized patients. There was no mortality in these series. Only 1.9% of patients required admission after the procedure. True complications were recorded in only 0.22% of the cases. Hospitalization was not necessary in 1753 patients (98%). From a statistical stand point, this represents savings of $313,588.00, based on expenses of approximately $30,000.00 for the payment of nursing personnel to run the unit, substracted form the total savings of... $343,588.00

Description of the Ambulatory Surgery Program

The objectives of this program are to perform a series of surgical procedures under anesthesia without the need of hospitalization, to offer post anesthesia care to the ambulatory patients providing the same safety given to hospitalized patients and to reduce the cost of hospitalization.

Patients that qualify for service in the program are those under 40 years of age who are to undergo a short surgical procedure under general or local anesthesia. Patients older than 40 years of age, will receive local anesthesia only. It should be understood that the concept of local anesthesia includes the supervision of anesthesia department and the possible use of neuroleptic agents.

Pre-operative evaluation of the patients is carried out on the out-patient clinic where a short history and physical examination are done and pertinent laboratory studies including Hgb, Hct., WBC, urinalysis and a chest film are ordered. Other laboratory tests are ordered as indicated.

On the day of surgery patients are admitted to the Ambulatory Surgery Unit. This unit consists of six beds under the supervision of registered and practical nurses. Once the patient is admitted, local preparation is carried out, and pre-medication is administered. The patients are taken to the operating room (O.R.) by the O.R. personnel, the sam' as an hospitalized patient. After the surgical procedure is completed, the patient is taken to the recovery room for observation. Upon discharge by the anesthesiologist, he is returned by Recovery Room personnel to the Ambulatory Surgery Unit, where he is re-evaluated and discharged by the surgeon receiving the instructions to be followed at home.

In those cases where the anesthesiologist and/or the surgeon determines that an additional period of observation is neccesary, admission to the hospital is carried out.

Experience Review

A total of 868 patients were operated by the General Surgery Service (Table 1). The most frequent procedures

TABLE I

Ambulatory Surgery — General Surgery				
	Anesthesia			
	Local	General	Total	Admitted
Excision of Mass	364	69	433	4
Breast Biopsy	47	72	119	6
Excision of ganglion cyst	16	68	74	1
Inguinal herniorraphy		66	66	1
Epigastric herniorraphy		42	42	1
Removal of foreign bodies	21	10	31	2
Rectal Wall Biopsy	1	14	15	1
Excision of anal polyp	3	6	9	1
Anal dilatation		5	5	
Others	28	36	64	1
TOTAL	480	388	868	18
	55%	45%		2%

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performed were excision of a mass-433 (364 under local anesthesia and 69 under general anesthesia), excision of ganglion cyst-74 (16 under local anesthesia and 68 under general anesthesia), inguinal hernirraphy 66, all under general anesthesia; epigastric herniorraphy 42, all under general anesthesia. Four hundred eighty or 55% were done under local anesthesia and 388 or 45% under general anesthesia. Hospitalization was necessary in 18 patients, or 2%.

The next table (Table 2) shows the experience of the Orthopedics Service. A total of 132 procedures were done, the most frequent were remanipulation of simple fractures-115, all under general anesthesia. Only 3 (2.2%) patients were admitted to the hospital.

TABLE II

Ambulatory Surgery — Orthopedics

	Anesthesia			
	Local	General	Total	Admitted
Remanipulation		115	115	2
Extraction of pin	2	10	12	1
Others	3	2	5	
TOTAL	5	127	132	3
	3.3%	96.2%		2.2%

The experience of the ENT Service is shown in Table 3. A total of 182 procedures were done, 131 (71.9%) under local anesthesia and 51 (28.9%) under general anesthesia. The most common procedures done in order of frequency were esophagoscopy, esophagoscopy and biopsy, dilatation of esophagus, laringoscopy and removal of foreign bodies. Only two patients (1%) were admitted.

TABLE III

Ambulatory Surgery-ENT

	Anesthesia			
	Local	General	Total	Admitted
Dilatation of esophagus	34	—	34	
Esophagoscopy	32	1	33	1
Removal of foreign body	4	18	22	
Laringoscopy	13	3	16	
Removal of vocal cord polyps	9	1	10	
Esphagoscopy biopsy	4	—	4	
Bronchoscopy	4	—	4	
Others	26	28	54	1
TOTAL	131	51	182	2
	71.9%	28.9%		1%

The Ophtalmology Service (Table 4) performed 177 procedures, 174 (98.4%) under local anesthesia and 3 (1.6%) under general. The most common procedure done was excision of pterygium. No patients were admitted.

TABLE IV

Ambulatory Surgery — Ophtalmology

	Anesthesia		
	Local	General	Total Admitted
Excision of pterygium	163	—	163
Excision of chalazion	6	—	6
Others	5	3	8
TOTAL	174	3	177
	98%.4%	1.6%	

The experience of the Urology Service (Table 5) shows a total of 428 procedures, 123 (29%) under local anesthesia and 305 (71%) under general anesthesia. The most common procedures were circumcisions on 290, all under general anesthesia; and cystoscopy, 126, all except 7, under local anesthesia. Eleven patients (2.5%) were admitted.

TABLE V

Ambulatory Surgery-Urology

	Anesthesia			
	Local	General	Total	Admitted
Circumcision		290	290	10
Cystoscopy	119	7	126	1
Ligation vas deferens	1	3	4	
Others	3	5	8	
TOTAL	123	305	428	11
	29%	71%		2.5%

The total experience is summarized in Table 6. A total of 1,787 cases were operated during the three-year period. Nine hundred thirteen cases were done under local anesthesia and 874 cases were done under general anesthesia. A total of 24 patients (1.9%) required admission to the hospital.

TABLE VI

Ambulatory Surgery
Total Experience (1977-78-79)

	Total	Local	General
General surgery	868	480	388
Orthopedics	132	5	127
ENT	182	131	51
Ophtalmololgy	177	174	3
Urology	428	123	305
TOTAL	1,787	913 (51%)	874 (49%)
Admitted to hospital 24 patients. (1.9%.)			

The records of twenty one patients that required admission were available for study. True complications of the surgical procedure were recorded in 4 cases (0.22%) Table 7. Two patients developed fever, that subsided spontaneously. One patient developed cardiac arrythmia during the procedure, and another patient had bleeding post circumcision in the recovery room. Five patients (0.28%) were admitted by order of the anesthesiologist because the procedure done required endotracheal anesthesia. Twelve patients (0.67%) were admitted for further observation because the procedure lasted longer than expected or was delayed so that the period of post operative recovery was not completed by 5:00 p.m. when the unit closed.

TABLE VII

Ambulatory Surgery Patients Requiring Admission (21 Cases)		
True complications:	4	(0.22%)
Fever: 2 Arrhythmia: 1 Bleeding: 1		
Anesthesia (Endotracheal)	5	(0.28%)
Observation	12	(0.67%)

The possible hospital savings were tabulated based on an average hospital routine where patients are admitted the night before surgery and remain in the hospital 24 hours after the procedure (See Table 8). The total savings for the 1,753 patients that were not admitted was $343,588.00.

TABLE VIII

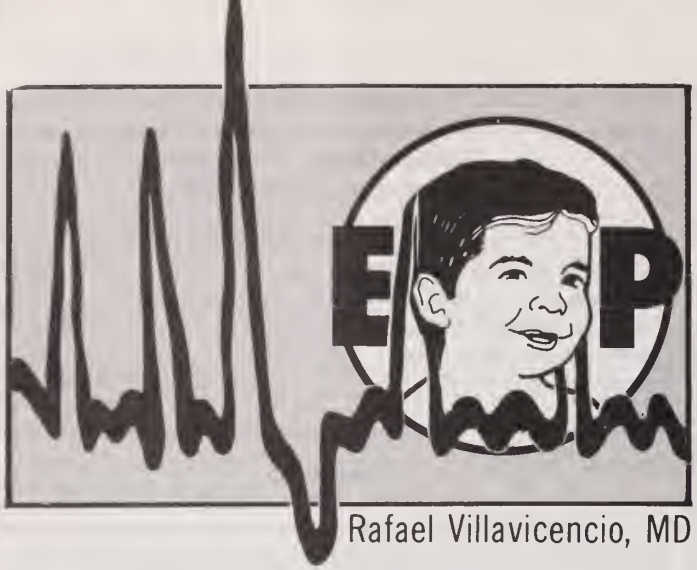
AMBULATORY SURGERY HOSPITALIZATION COSTS	
Total number of patients	1,787
Patients not required admission	1,753
Average hospital stay	2 days
Average per diem cost	$98.00
Total cost	$343,588.00

Resumen

Este estudio se llevó a cabo para evaluar los resultados del Programa de Cirugía Ambulatoria del Hospital Regional de Ponce, durante un período de tres (3) años (1977-80). Un total de 1,787 pacientes fueron intervenidos quirúrgicamente recibiendo anestesia general o local suplementado por neuroleptos y bajo la supervisión de un anestesiólogo.

Se expone una breve descripción de la organización de la Unidad de Cirugía Ambulatoria y se evalúan los resultados de acuerdo al tipo de cirugía llevada a cabo, la presencia o ausencia de complicaciones y la necesidad de hospitalización en estos pacientes.

El estudio demuestra que los pacientes recibieron el mismo tipo de tratamiento usualmente dado a pacientes hospitalizados. No hubo mortalidad en al serie. Complicaciones verdaderas fueron encontradas en solamente 0.22% de los casos. La hospitalización fue requerida únicamente en el 1.9% de los pacientes, lo que significa que la hospitalización no fue necesaria en 1,753 pacientes (98%). Desde el punto de vista estadístico, esto representó un ahorro de $313,588.00 basado en gastos de aproximadamente $30,000.00 para el pago de personal de enfermería a cargo de la unidad, restado del ahorto total de...$343,588.00...



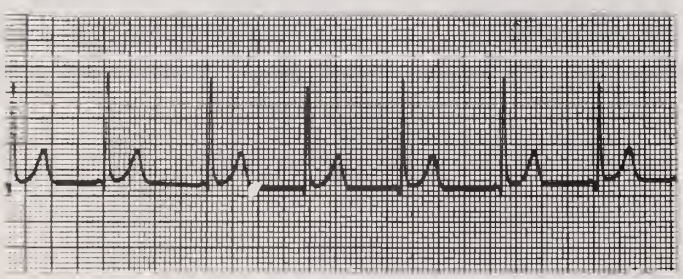
Rafael Villavicencio, MD

Sección de Autoevaluación

ELECTROCARDIOGRAFIA PEDIATRICA

DRM es un niño de 10 años de edad referido para evaluación de episodios de "taquicardia". Estos son de aparición súbita y corta duración con un cese abrupto. No se relacionan con el ejercicio así como tampoco ocasionan mareos, diaforesis, ni síncope.

El historial médico pasado del niño no es significativo y su examen físico es normal al igual que las pruebas de función tiroidea y tolerancia de glucosa. La radiografía de torax fue normal y la derivación II del electrocardiograma (ECG) en reposo se ilustra a continuación:



El hallazgo electrocardiográfico más significativo es:

a) arritmia sinusal
b) ondas R amplias
c) intervalo QRS amplio
d) intervalo PR corto
e) onda "q" patológica

Respuesta

d): Intervalo PR corto

El intervalo PR es la traducción electrocardiográfica del tiempo que le toma al impulso cardíaco llegar a las fibras musculares ventriculares desde el nodo sinusal a través del tejido especializado de conducción.

En el ECG de superficie este intervalo se mide desde el comienzo de la onda P al comienzo de la onda R, o la onda Q si no hay R.

La duración del intervalo PR varía según la *frecuencia cardíaca* y la *edad* del paciente y sus alteraciones pueden ser datos de considerable importancia en el diagnóstico o en el pronóstico de ciertos trastornos cardíacos. También podemos ver acortamiento o prolongación del intervalo PR en un porciento de la población normal.

Análisis del Trazado

El trazado que presentamos revela un ritmo sinusal, regular, con una frecuencia cardíaca de 85/min. Los intervalos QRS son de configuración, amplitud, y duración normal. El intervalo PR es como podemos ver anormalmente corto. Su duración es de 0.08 sec. cuando para la edad y frecuencia cardíaca del paciente no debía ser menor de 0.12 sec. ni mayor de 0.17 sec.[1].

Situaciones Clínicas

Las catecolaminas circulantes, el tono autonómico, y algunos agentes farmacológicos pueden producir un tiempo de conducción A-V acortado, pero funcionalmente normal.

También podemos encontrar un intervalo PR acortado en:

a) Infantes normales menores de 6 meses de edad.
b) Enfermedad de Pompe - tesaurismosis de glucógeno tipo II.
c) Presencia de marcapasos ectópicos.
d) Síndrome de Lown-Ganong-Levine (LGL).

Síndrome de Lown-Ganong-Levine

Son pacientes con intervalo PR corto, intervalo QRS normal (onda delta ausente) y predisposición a taquicardia. Estos pacientes tienen tractos accesorios que crean un corto circuito entre el nodo AV y el haz de His y también se han descrito cortos circuitos en el propio nodo atrioventricular.[2] Debido a que en estas circunstancias se obvia la conducción a través del área donde normalmente se retrasa el impulso (nodo A-V), estos pacientes demuestran característicamente un intervalo AH corto. Debe aclararse que en los pacientes con intérvalo PR anormalmente corto no se debe dar por sentado la presencia de un tracto accesorio hasta tanto no se haya podido confirmar mediante estudios electrofisiológicos invasivos.

Las disritmias más frecuentes en los pacientes con el síndrome de LGL son taquicardia supraventricular (50%); taquicardia ventricular (33%), y fibrilación atrial (17%).[3] El fundamento para la asociación de un intervalo PR corto y estas taquidisritmias no está aclarado por completo.

Mecanismo

El intervalo PR corto en pacientes con LGL resulta principalmente de un acortamiento del intervalo AH. El período refractario del nodo A-V también se acorta en los paciente con LGL. Sin embargo, aunque este período refractario es más corto que en los pacientes con intervalo PR normal, es igualmente corto en aquellos con intervalo PR anormalmente corto sin historial de taquidisritmias.[4] Estas características de la conducción A-V y de la refractariedad en los pacientes con intervalo PR corto facilitan el que se produzca taquicardia y pueden explicar el porqué estos pacientes desarrollan síntomas.

El diagnóstico de LGL se logra mediante la realización de estudios electrofisiológicos invasivos. Esta es una de las principales razones por la cual la verdadera incidencia del síndrome se desconoce.

Con la presentación de este ECG se pretende darle la relevancia que el síndrome se merece. Debemos tener en mente el LGL en aquellos pacientes con PR corto y QRS normal que informen sobre "episodios de taquicardia" aunque clínicamente se encuentren bien compensados desde el punto de vista cardiovascular y asintomáticos. En este caso solo se recomienda observación, evitar la estimulación adrenérgica y vigilar para la aparición taquidisritmias.

Si aparecen, el tratamiento es el mismo que para el síndrome de Wolff-Parkinson-White.

Si la respuesta al tratamiento médico no es satisfactoria, se debe proceder a la realización de estudios electrofisiológicos invasivos. De esta forma se determinará el mecanismo que ocasiona la disritmia y se comenzará el tratamiento de acuerdo a los hallazgos del mismo.

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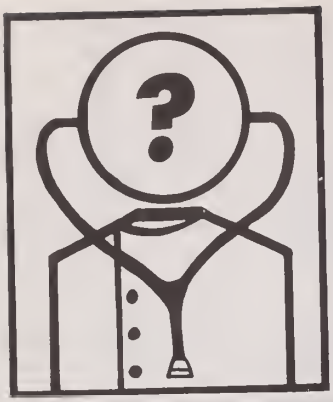
La foto muestra el pueblo de Guánica en 1899 y el calce lee: "Este es el lugar del desembarco de las tropas americanas, el 25 de julio de 1898. Está en la costa sur, como a 20 millas al oeste de Ponce".

Fotografía cortesía de Dolores Mendez-Cashion, M.D.



José Rivera del Río, MD

Cúal es su Diagnóstico

El paciente que presentaremos a continuación es un varón de 28 años de edad con un soplo sistólico eyectivo grado 2/VI en el foco pulmonar. En su evaluación médica encontramos un historial pasado completamente no contributorio y un paciente asintomático. En el examen físico observamos un pulso venoso yugular normal, un ápice cardíaco que se palpa en el quinto espacio intercostal contra la línea media-clavicular izquierda sin frémito. Un aumento en el segundo sonido es palpable en foco pulmonar. La auscultación revela un segundo sonido (P2) fuerte, un desdoblamiento fisiológico y un soplo sistólico eyectivo grado 2-3/VI en el foco pulmonar sin irradiación a las carótidas. En el mismo foco detectamos un "click" (sonido de eyección) sistólico que disminuye con la inspiración. La maniobra de Valsalva y el ponerse en cuclillas disminuyen el soplo.

El electrocardiograma es normal (Fig. 1) y la radiografía de tórax aparece en la Figura 2.

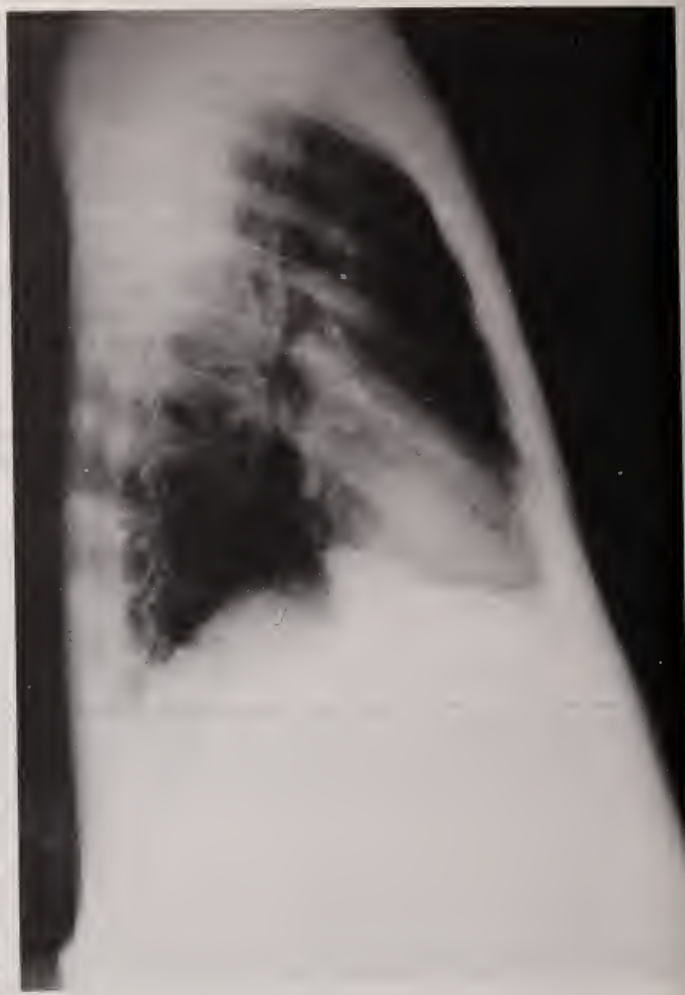


Fig. 2

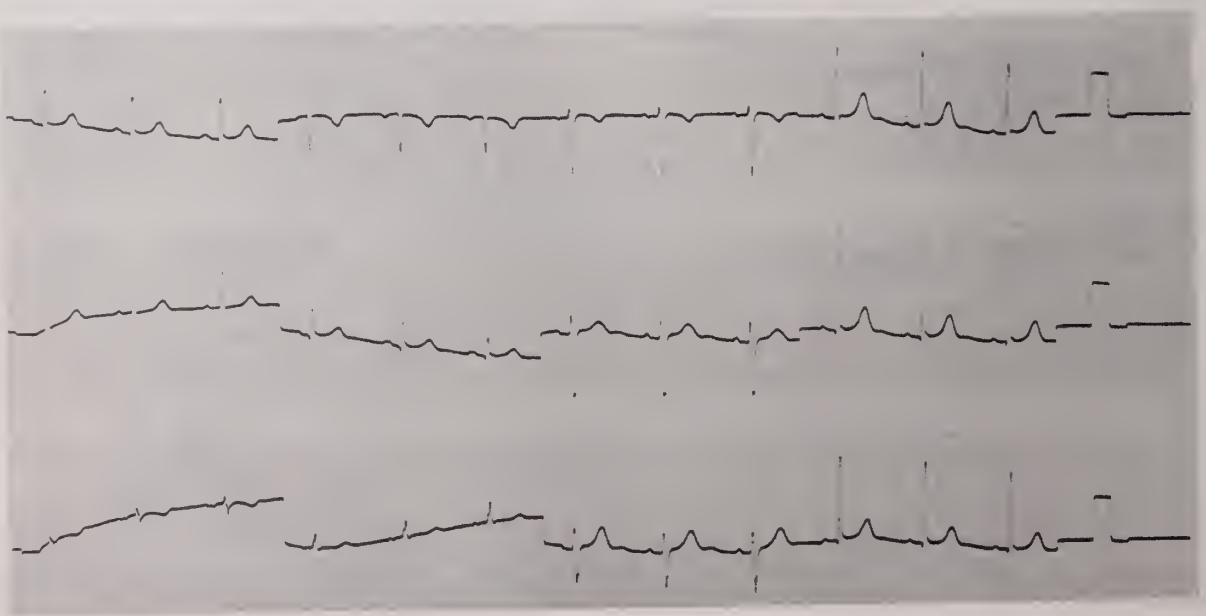


Fig. 1

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The Physician's Sleep Glossary

Some common sleep laboratory terms

poly•som•no•graph. An instrument which simultaneously records by electrodes physiological variables during sleep—for example, brain activity (EEG), eye movements (EOG), muscle tonus (EMG) and other electrophysiological variables. These readings indicate precisely when patients fall asleep, how many wake periods they experience, the quality of sleep and the duration of sleep.

sleep la•ten•cy. The period of time measured from "lights out," or bedtime, to the commencement or onset of sleep.

wake time af•ter sleep on•set. Intervals of time spent awake between onset of sleep and the end of the sleep period. The polysomnograph registers the length and frequency of the intervals.

to•tal sleep time. The amount of time actually spent in sleeping. This is estimated by subtracting wake times from the period encompassed by the onset and the termination of sleep.[1]

REM/NREM. 1. REM, or rapid eye movement, sleep is "active"—characterized by increased metabolic rates, elevated temperature and arousal-type EEG patterns. 2. NREM, or non-rapid eye movement, sleep represents "quiet" sleep stages. There are four distinct stages of NREM sleep.[2]

re•bound in•som•nia. A statistically significant worsening of sleep compared to baseline on the nights immediately following discontinuation of sleep medication.[3]

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The efficacy of Dalmane has been studied in over 200 clinical trials with more than 10,000 patients.[3-15] During long-term therapy, which is rarely required, periodic blood, kidney and liver function tests should be performed. Contraindicated in patients who are pregnant or hypersensitive to flurazepam.

Please see summary of product information on following page.

References: 1. Williams RL, Karacan I: Introduction, chap. 1, in *Sleep Disorders: Diagnosis and Treatment*, edited by Williams RL, Karacan I, Frazier SH. New York, John Wiley & Sons, 1978, p. 2. **2.** Data on file, Hoffmann-La Roche Inc., Nutley, NJ. **3.** Kales A *et al: JAMA 241*:1692-1695, Apr 20, 1979. **4.** Kales A *et al: J Clin Pharmacol 17*:207-213, Apr 1977 and data on file, Hoffmann-La Roche Inc., Nutley, NJ. **5.** Kales A: Data on file, Hoffmann-La Roche Inc., Nutley, NJ. **6.** Kales A *et al: Clin Pharmacol Ther 19*:576-583, May 1976. **7.** Kales A, Scharf MB, Kales JD: *Science 201*:1039-1041, Sep 15, 1978. **8.** Frost JD Jr, DeLucchi MR: *J Am Geriatr Soc 27*:541-546, Dec 1979. **9.** Dement WC *et al: Behav Med 5*(10):25-31, Oct 1978. **10.** Vogel GW: Data on file, Hoffmann-La Roche Inc., Nutley, NJ. **11.** Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington, DC, May 3-7, 1971. **12.** Pollak CP, McGregor PA, Weitzman ED: The effects of flurazepam on daytime sleep after acute sleep-wake cycle reversal. Presented at the 15th annual meeting of the Association for Psychophysiological Study of Sleep, Edinburgh, Scotland, June 30-July 4, 1975. **13.** Zimmerman AM: *Curr Ther Res 13*:18-22, Jan 1971. **14.** Kales A, Kales JD: *Pharmacol Physicians 4*(9):1-6, Sep 1970. **15.** Data on file, Hoffmann-La Roche Inc., Nutley, NJ.

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Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; in acute or chronic medical situations requiring restful sleep. Objective sleep laboratory data have shown effectiveness for at least 28 consecutive nights of administration. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended. Repeated therapy should only be undertaken with appropriate patient evaluation.

Contraindications: Known hypersensitivity to flurazepam HCl; pregnancy. Benzodiazepines may cause fetal damage when administered during pregnancy. Several studies suggest an increased risk of congenital malformations associated with benzodiazepine use during the first trimester. Warn patients of the potential risks to the fetus should the possibility of becoming pregnant exist while receiving flurazepam. Instruct patient to discontinue drug prior to becoming pregnant. Consider the possibility of pregnancy prior to instituting therapy.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nighttime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressants. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg recommended initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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El diagnóstico correcto es:

a) Defecto interatrial
b) Estenosis pulmonar
c) Síndrome de la espalda recta ("straight back syndrome")
d) Estenosis aórtica

Contestación: C.

Discusión

Este síndrome, llamado así por la ausencia de la cifosis dorsal con la consecuente producción de una espalda recta, ha sido causa de confusión diagnóstica en muchas ocasiones. Esta "rectitud" causa la pérdida de dimensiones anteroposteriores torácicas desplazando el corazón y comprimiendo su parte anterior contra el esternón.

Esta comprensión repercute sobre la arteria pulmonar haciendo que el paso del flujo sanguíneo sea turbulento con la consecuente producción del soplo (usualmente eyectivo, temprano-medial y grado 2-3/VI), ocasionalmente un "click", y muy raramente fremito táctil. La proximidad del corazón para con el foco pulmonar justifica el aumento del segundo sonido.

El electrocardiograma es usualmente normal. También pueden estar presentes ondas "r" secundarias rSr^{1} en las derivaciones precordiales derechas así como cambios inespecíficos en las ondas "T".

A pesar de verse claramente su deformidad torácica, estos pacientes usualmente están asintomáticos. Otros síntomas referentes a defectos interatriales o prolapso de válvula mitral coexisten ocasionalmente.

En su diagnóstico diferencial se incluye: estenosis pulmonar, estenosis aórtica, dilatación idiopática de la arteria pulmonar y la comunicación interatrial.

Considerando que los estudios angiográficos y hemodinámicos han descartado la presencia de enfermedad cardíaca, es deber del médico el aclararle al paciente la ausencia de enfermedad en este síndrome de aparición frecuente y esporádicamente diagnosticado.

DECLARACION RESPECTO AL MAL USO GLOBAL DE ANTIBIOTICOS

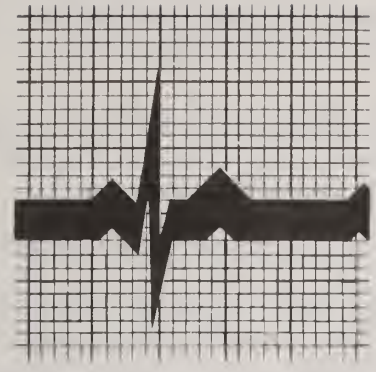
Los antibióticos han sido emplazados para tratar enfermedades en hombres, animales y plantas, causadas por microorganismos. Sin embargo, estos agentes antimicrobianos están perdiendo eficacia por la diseminación y persistencia de organismos resistentes a ellos. Además, de no tomarse medidas para limitar la situación actual, llegará el momento en que los antibióticos no sean útiles para el combate de enfermedades.

Ya vivimos un problema de salud pública a nivel mundial, causado en parte por el empleo de antibióticos sin medida, por lo siguiente: a) la venta de antibióticos sin prescripción médica; b) el empleo de antibióticos útiles en medicina humana como promotores del crecimiento en alimentación animal y en agricultura; c) la precripción de antibióticos en padecimientos en los que son ineficaces; d) el engaño al consumidor, al anunciar antibióticos como "drogas mágicas," especialmente en áreas en las que la venta no está legislada; e) el uso de distintos nombres y de propaganda para la venta del mismo producto en diferentes partes del mundo.

De ninguna manera el uso generalizado de antibióticos es un substitutivo para el buen saneamiento y la higiene personal. Deben fomentarse y fortalecerse los esfuerzos para mejorar estos principios de prevención y control de enfermedades infecciosas. Al mismo tiempo, es urgente incrementar el conocimiento de las consecuencias peligrosas del mal uso de antibióticos a todos los niveles: consumidores, médicos, vendedores, fabricantes y dependencias gubernamentales. Sólo así podremos iniciar el establecimiento de medidas que limiten el uso innecesario y el mal uso de estos agentes.

Los abajo firmantes hemos escrito esta declaración para promover acciones que limiten este problema global que tiende a incrementare. Quisiéramos que esta comunicación sirva como impulso para la organización de comités nacionales e internacionales de los que emanen normas de dirección para establecer el uso prudente de antibióticos. como primer paso, instamos que que se implante y se cumpla un sistema uniforme en la prescripción y distribución de antibióticos en aquellas áreas en las que ya hay personal médico experto. Además, exhortamos a que establezcan estándares de propaganda y de venta de estos fármacos y que las naciones del mundo cumplan con ellos.

La declaración anterior emergió de presentaciones y discusiones durante la Conferencia sobre Biología Molecular, Patogenicidad y Ecología de Plásmidos celebrada en Santo Domingo, República Dominicana, en enero de 1981. Los que firmaron lo hicieron como individuos y no como representantes de sus instituciones, y fueron de los siguientes países: República Federal Alemana, 9; México 6; EE.UU., 83; Japón, 4; Inglaterra, 9; Irlanda, 1; Suecia, 4; España, 3; Brasil, 2; Canadá, 4; Suiza, 1; Israel, 2; Guatemala, 1; Colombia, 1; Austria, 1; Francia, 1; Italia, 3; Venezuela, 1; República Dominicana, 2; Finlandia, 1; Grecia, 1; Holanda, 2; Dinamarca, 1; Turquía, 1; Escocia, 1; Uruguay, 1.



ELECTROCARDIOGRAM OF THE MONTH

Rheumatic Mitral Stenosis In Association With The Short P-R Normal QRS Syndrome

Charles D. Johnson, M.D.

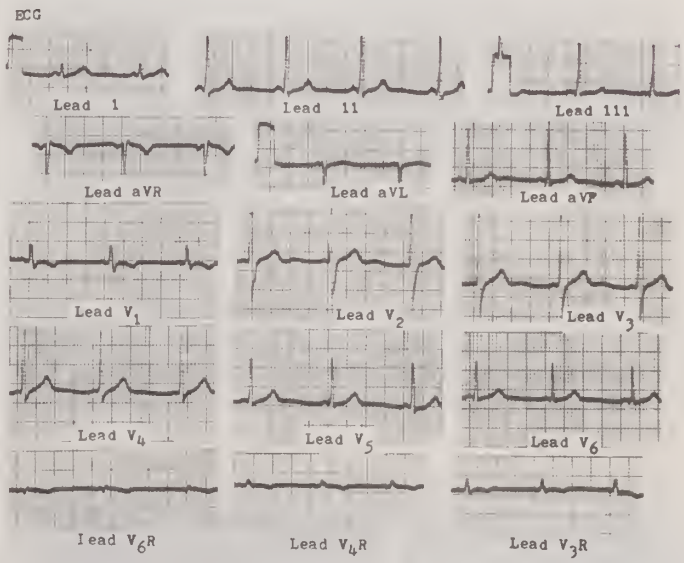
This 26-year-old female suffered rheumatic fever (RF) as a child. Increasing symptoms of dizziness, palpitations, dyspnea and chest pains ensued. Physical examination revealed an anxious young woman with a loud first heart sound, an opening snap, a grade 3 diastolic rumble with presystolic accentuation and a grade 1 apical systolic murmur. Cardiac catheterizations at ages 26 and 29 years revealed mild mitral stenosis (MS): mean mitral diastolic gradients were 12 and 21 mm Hg, 5 end-diastolic; mean wedge 15, with a wave 22, v wave 19 mm Hg; the calculated mitral valve area was 1.58 cm^2; pulmonary artery 34/14, mean 23 and right ventricular pressure 34/5 and 44/10 mm Hg; the total pulmonary arterial resistance was 527 and the arteriolar resistance 165 dynes-S-cm^{-5}. Angiograms showed a bicuspid aortic valve, thickened mitral valve and mild mitral regurgitation (MR). Digoxin and propranolol were rescribed. Her symptoms of dyspnea, orthopnea, leg edema, nervousness, tachycardia, diarrhea, sweating and heat intolerance increased. At open commissurotomy, age 29, there were a small left atrium and finger-tip MS with commissural fusion but relatively thin leaflets. She improved slightly but has continued with palpitations, dyspnea, chest pains, sweating, headaches, etc. Thyroid function studies were negative.

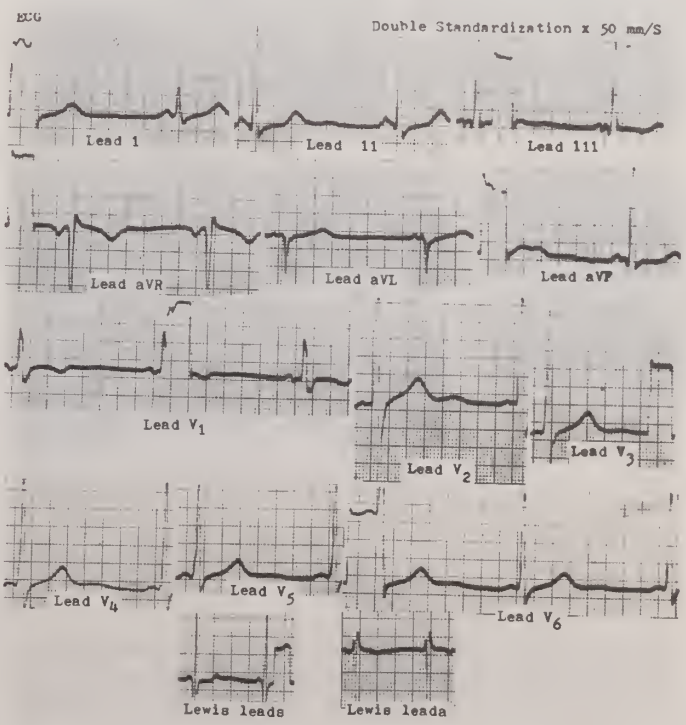
Electrocardiograms (ECG).

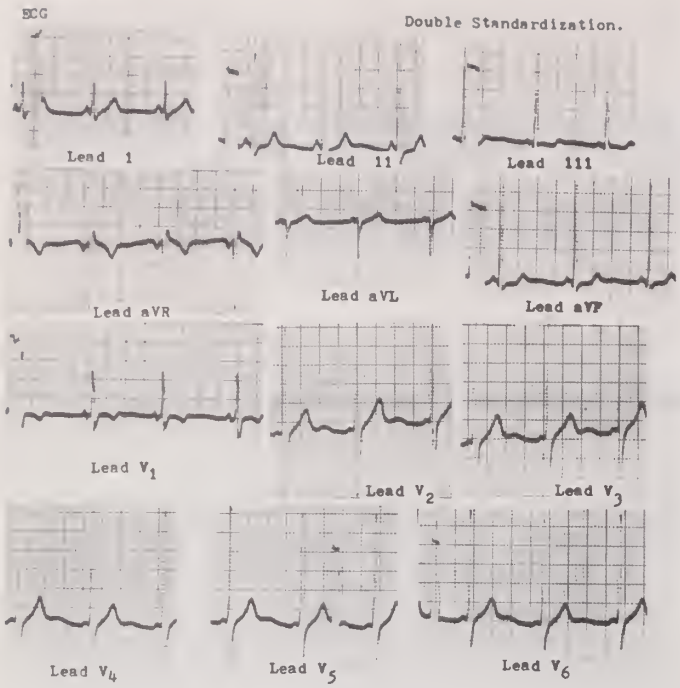
Figures 1, 2 and 3 reveal a short P-R interval of 0.09 S, QRS 0.10 S, axis + 80º; the R/S ratio is 1 from lead V_4R to V_6. Only minimal slur or curvature of the R wave upstroke is detectable. There was a Rsr' complex in V_1 on one trace.

Vectorcardiogram (Frank)

There are anteriorly (approximately 2/3 of loop, maximal horizontal (H) QRS vector + 40º) located loops with normal rotation. No definite delta wave is identified in the loops or in the orthogonal leads. Efferent velocity is

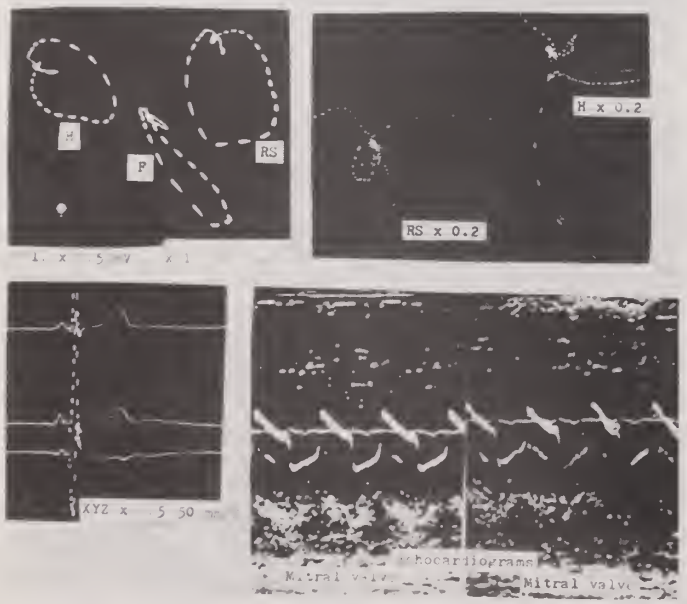






slightly slower than afferent. Slight terminal QRS slowing is present. The H T loop is rotating clockwise.

The postoperative ECG showed a nearer equiphasic R/S complex in lead V, and an inverted T wave. The P-R interval remained short.



Comments

The Wolff-Parkinson-White (WPW) or Preexcitation syndrome has been documented in association with numerous congenital and acquired cardiac and noncardiac diseases. In many of these the association may be only coincidental as the syndrome has a 0.1 — 0.4% incidence in routine electrocardiographic tracings and 1.6 per thousand in the general population. These associations may be classified as follows:

I. Congenital heart defects (in 33 to 50% of all children with preexcitation).
Ebstein's anomaly, in 5-25% of cases, type B.
Tricuspid atresia
Transposition of the great arteries (TGA) and corrected TGA.
Ventricular septal defect, secundum atrial septal defect, patent ductus arteriosus, valvular pulmonic stenosis, mitral atresia.
Tetralogy and Pentalogy of Fallot
Dextrocardia, dextroversion, partial or total situs inversus.
Coarctation of aorta. Subaortic stenosis, discrete or muscular.
Endocardial fibroelastosis. Double-outlet and double-inlet right ventricle. Eisenmenger complex. Diverticulum of pericardium.

II. Atherosclerotic heart disease
Myocardial infarction, coronary insufficiency, ischemia, angina

III. Cardiomyopathy
Familial. Hypertrophic obstructive, nonobstructive, congestive.

IV. Hypertensive and Syphilitic heart diseases. Acute pericarditis.
Pompe's disease. Hypoxemia testing.

V. Mitral valve prolapse

VI. Sick sinus syndrome

VII. Marfan's syndrome

VIII. Thyrotoxicosis

IX. Psychoneurosis, paroxysmal cerebral disorders, epilepsy, vegetative nervous system lability, cerebral circulatory disturbances. Mental retardation, visual loss, optic atrophy, etc.
Friedrich's ataxia. Duchenne's muscular dystrophy. Charcot-Marie-Tooth's disease. Myasthenia.

X. Respiratory infections.

XI. Acute RF. Myocarditis. Rheumatic Heart Disease (RHD). Bain, in 1926, observed Type A WPW in a 10-year-old male with RHD and an apical systolic murmur. Meneely, in 1949, reported a 10-year-old male with a mitral systolic murmur in acute RF, and he cited other previous reports by Bishop, Humber, Willius and Mahaim. Blom, in 1951, saw a 22-year-old male with RHD and aortic insufficiency, and Rodstein a 15-year-old male with a history of RF, atrioventricular block and a systolic murmur at the pulmonic area. Schiebler, in 1959, observed a 15-year-old male with rheumatic carditis, MR and dull intelligence. Apostolov reported a 32-year-old male tith RHD, stenosis and insufficiency of the mitral and aortic valves, atrial fibrillation/further with pseudo-ventricular tachycardia. Autopsy showed recrudescent rheumocarditis and fibrous changes in the interventricular septum and cardiac apex. The authors emphasized the rheumatic etiopathogenesis of the WPW syndrome, which has received credence in the past by other authorities. Sherf & Neufeld have published examples of this association. Their Figure 9 shows disappearance of the

R wave in V_1 and greater left axis deviation after mitral commissurotomy.

Prominent Anterior Forces in the Right Precordial leads.

Dominant R waves or RSR' complexes in the right precordial leads may occur in several conditions:

1. Normal (5%), a vertical heart, pectus excavatum, extreme counterclockwise (CCW) rotation.
2. Wilson's central terminal error.
3. Incomplete and complete right bundle branch block.
4. Dorsal (high posterior) and posterolateral myocardial infarctions.
5. Left ventricular hypertrophy and dilatation, with diastolic overload, and CCW rotation.
6. Duchenne's muscular dystrophy
7. Constrictive pericarditis
8. Ventricular Tachycardia (VT).
9. Left posterior and anterior hemiblocks. Right ventricular conduction disturbance. Left septal fascicular block (anterior conduction delay), ischemic heart disease, papillary muscle dysfunction; hypertrophic obstructive and nonobstructive cardiomyopathy.
10. Right ventricular hypertrophy (RVH), acute cor pulmonale.
11. Lown-Ganong-Levine ((LGL) syndrome (doubtful).
12. Type A (and B) WPW syndrome.

Arrythmias were not documented electrocardiographically in this patient but were suggested by the history. Any delta wave was equivocal. So, the best designation in this controversial area may be the Short P-R and Normal QRS symdrome

The LGL syndrome refers to a short P-R interval and normal QRS complex associated with paroxysmal rapid heart action. Lown et al believed it to be a distinct entity but many authorities regard it as a WPW syndrome variant, and it is often included in the Preexcitation or Accelerated AV conduction syndromes.

Short P-R intervals may exist with our without tachycardia; only 11% of Lown et al 200 patients with short P-R intervals demonstrated tachycardias. Sherf observed an incidence of short P-R and normal QRS complex in 0.4 - 2% of apparently normal adults. For most, it is a loose synonym for all kinds of short P-R's.

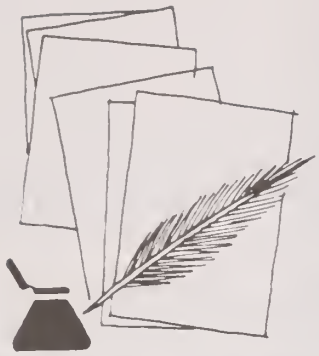
Because of these disarrays, it has been proposed that the term LGL syndrome be dropped in favor of the above designated phrase.

Among various possible etiologies, atrio-hisian (James) fiber conduction presently enjoys popularity. A delta wave is not definite, but even a classic WPW syndrome may not present a clear delta wave. Coronary nodal rhythm also is identical except for lack of tachyarrythmias.

Noteworthy supporting evidence is that laboratory studies in patients with short P-R intervals but without symptomatic cardiac arrythmias have revealed electrophysiologic features indistinguishable from those recorded in patients with the LGL syndrome.

Mild RHV can explain the prominent anterior forces. Thus, mild RHV due to rheumatic mitral stenosis in combination with the Short P-R, normal QRS syndrome, may best explain this interesting dilemma and vignette. The persistence of her previous symptoms, the short P-R interval and a less prominent R/S ratio in V_1 postoperatively, favor this conclusion.

(References will be submitted upon request to the author)



CARTAS AL EDITOR

Factores Para Determinar Riesgos de Cáncer

Me permito incluirle el resumen más breve de factores para estimar riesgos de desarrollar cáncer de las siete localizaciones más frecuentes en Puerto Rico.

FACTORES PARA DETERMINAR SU RIESGO DE CANCER

	Pulmón	Seno	Utero (Endometrio)	Cuello Uterino	Esófago	Estómago	Colon
RIESGO MODERADO (2-3 veces)	Fumar 5-9 cigarrillos por día o Historial familiar de este cáncer (padres, hermanos o hermanas)	Historial familiar de este cáncer (madre, hermanas) o Posiblemente dieta alta en grasas o Menopausia después de los 52 u Obesidad o Tener su primer hijo después de los 30 años de edad o No tener hijos.	Historial familiar (hermanas, madre) o Menopausia después de 52 años de edad o Sobrepeso moderado o No haber tenido hijos o Haber recibido estrógenos en dosis moderadas.	Muchos compañeros sexuales o Tener relaciones sexuales tempranamente (antes de los 18 años de edad)	Fuerte consumo de alcohol (más de tres tragos de 2 oz. de 80° Prueba, por día, o su equivalente en vino o cerveza) o Fumar un paquete de cigarrillos.	Historial familiar (padres, hermanos o hermanas) o Consumo frecuente de pescado ahumado o seco, vegetales preservados en vinagre.	Historial familiar (padres, hermanos o hermanas) o Dieta alta en proteínas o alta en grasas.
RIESGO GRANDE (4 veces mayor)	Historial familiar de este cáncer y fumar de 1-9 cigarrillos por día o Fumar 10 ó más cigarrillos por día	Dos o más factores de riesgo de cáncer del pechu	Obesidad o una combinación de dos o más de los otros factores de cáncer uterino o Terapia con estrógenos, dosis altas y por largo tiempo.	Primeras relaciones sexuales antes de los 18 años de edad y muchos compañeros sexuales	Fumar un paquete de cigarrillos o más y consumo fuerte de alcohol	Una combinación de factores de riesgo de cáncer del estómago o Anemia perniciosa, gastritis o diabetes	Colitis ulcerativa o una combinación de dos factores de cáncer del colon de arriba.

Fuente: Drs. Elizabeth Whelan & Philip Cole, Escuela de Salud Pública de Harvard.

Isidro Martínez, MD
Director
Programa Control del Cáncer

Radioimmunoassay Pregnancy Test

The serum pregnancy test by radioimmunoassay is considered a very sensitive and specific test for the early diagnosis of pregnancy. During the past few years we have noticed an alarming incidence of false positive tests as proved by serial sonographic examinations of the female pelvis. The falsely positive pregnancy test in view of a sonographically empty uterus raises the possibility of an ectopic gestation and the patient may be exposed to an unnecessary laparoscopy or laparatomy.

The serum radioimmunoassay determination of human chorionic gonadotropin (H.C.G.) involves a specific antibody reaction with the beta sub-unit of H.C.G. This test can be performed as a stat qualitative test or as a quantitative assay. The qualitative test is performed in about 2 hours while the quantitative assay may take 24 horus to be completed. In the qualitative test the patient's specimen is compared to a positive standard. Using this technique samples are classified as positive, negative or indeterminate. The samples falling in the indeterminate zone are non-diagnostic. Such patients should be retested in 48 hours at which time in a normal pregnancy the H.C.G. levels will have doubled in concentration. The quantitative test determines the exact amount of hormone present and is useful in cases of missed abortions and molar gestations.

The analytical techniques involved in these tests must be very carefully carried out in order to obtain reliable results. One possible technical source of error is an improper pipetting technique. A technologist testing several samples may have negative specimens as well as specimens containing extremely high amounts of H.C.G. If the technologist uses one of the types of pipets which is tranferred from specimen to specimen such as th commonly used S.M.I. pipet, the possibility of contaminating a negative specimen is high. Pipets with disposable tips which are changed after every specimen are essential for obtaining reliable results.

Other possible sources of error include testing of hyperlipemic specimens as well as specimens containing abnormally high protein levels. If the radioimmune assay is not specific for the beta sub-unit of H.C.G., cross reaction with lutenizing hormone (L.H.) may also yield false positive results.

The purpose of this communication is to alert the obstetricians of the high incidence of false positive R.I.A. pregnancy tests. Whenever the diagnosis of ectopic gestation is entertained a specific R.I.A. beta sub-unit quantitative pregnancy test should be requested. The test should be performed in a reliable laboratory and the physician should be aware of possible false positive results. A controlled study in search for other possible sources of error will be conducted in the near future under the supervision of the University of Puerto Rico, School of Medicine.

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Resumenes de La Literatura Médica

LA UTILIDAD DE LA MAMOGRAFIA EN LA EVALUACION DE PACIENTES CON CARCINOMA TEMPRANO DE LA MAMA POR TUMORECTOMIA Y RADIOTERAPIA. Gefter WB, Freedman AK, Goodman RL: Radiology 1982, 142:77.

El valor de la mamografía en la planificación del tratamiento de carcinoma temprano de la mama *anejo* de una biopsia excisional fue estudiado en 38 pacientes. Una tercera parte de las mamografías post-biopsia brindaron información útil para el tratamiento o seguimiento de estas pacientes, específicamente la presencia o ausencia de tumor residual y la detección de lesiones ocultas en la otra mama o en los nódulos linfáticos de la axila. Sirvieron también como estudio de referencia valioso ya que las cicatrices vistas en mamografías luego del tratamiento pueden similar tumor nuevo o recidiva. Aproximadamente la mitad de los estudios post-biopsia fueron no-diagnósticos debido a la densidad del parenquima mamario, o a la distorsión post-biopsia. Cuatro mamogramas fueron considerados falsos positivos para tumor residual. Estos resultados indican que la mamografía puede contribuir significativamente al manejo de pacientes sometidos a tumorectomía y radioterapia primaria por carcinoma de la mama.

La obtención de una mamografía rutinariamente *antes de* la biopsia y la posposición de la mamografía post-biopsia hasta tanto haya sanado la herida, aumentaría ciertamente el valor diagnóstico de esta evaluación.

Bernardo Marqués, MD

SKIN TESTING FOR PENICILLIN ALLERGY. Van Dellen RG: J Allergy Clin Immunol 1981; 68:169.

En este editorial sobre las pruebas cutáneas para alergia a la penicilina, el autor, (facultativo de la División de Enfermedades Alérgicas de la Clínica Mayo) señala que el uso de dichas pruebas por lo general se reserva para las personas con historia de alergia a la penicilina que sufren de una infección grave y necesitan el antibiótico. Las pruebas conllevan un pequeño riesgo. A veces dan reacciones generalizadas y hay por lo menos tres casos de muerte informados en la literatura debidas a las mismas. No todos los materiales necesarios para hacer las pruebas están disponibles comercialmente. La interpretación de los resultados es difícil; en el 9% de los casos no se pueden interpretar y en el 8% son equívocos.

José E. Sifontes, MD

THE ANNUAL CHEST ROENTGENOGRAM FOR THE CONTROL OF TUBERCULOSIS IN HOSPITAL EMPLOYEES: RECENT CHANGES AND THEIR IMPLICATIONS:Cope R,Harlstern AI.Am Rev Respir Dis 1982; 125:106.

En Oregón no se encontraron casos de tuberculosis en 571 empleados de hospitales que fueron sometidos a la radiografía de torax como rutina anual. Se encontraron 2 casos de tuberculosis en 39 que tenían la tuberculina positiva al solicitar el empleo y 1 de 30 que tuvo el viraje tuberculínico de negativo a positivo. Se concluye que en las personas con tuberculina positiva, después de una evaluación inicial, que incluye la radiografía de torax, no es productivo continuar las radiografías de rutina anualmente a menos que existan factores de riesgo en una persona tales como inmunosupresión y otros.

José E. Sifontes, MD

CONGENITAL MITRAL VALVE ANOMALIES IN TRANSPOSITION OF THE GREAT ARTERIES: Moene, RJ, Oppenheimer-Dekker A. Am J Cardiol 1982; 49:1972.

In this study the authors reviewed 165 cases with transposition of the great arteries (TGA) from the Pediatric Cardiology Section of the Free University Hospital in The Netherlands. They placed special emphasis in the morphology of the mitral valve, anomalies were described in 36 cases (22 percent) and they were divided into 4 groups:

Group A- 16 hearts with either partial or complete cleft in the anterior mitral valve leaflet. Severe outflow tract stenosis was present in 8 cases where the cleft was located anterior to the pulmonary ostium.

Group B- 8 specimens with abnormal size or position of the mitral valve, or both.

Group C- 7 specimens with redundant left ventricular structures involving the mitral valve.

Group D- 5 hearts with deficient papillary muscles.

The authors stress the importance in recognizing such anomalies which will cause dysfunction of the mitral valve apparatus. In such cases balloon septostomy will fail to produce significant mixing at atrial level and most important of all, such findings are extremely valuable for patients in whom

anatomical surgical correction of the TGV is contemplated.

In comparison with the Mustard procedure for repair of TGV the "arterial switch" operation makes greater demands on the integrity of the valve apparatus because the left ventricular pressure remains at systemic level.

They conclude that abnormal mitral valve is not unusual in patients with TGV, that such anomalies must be ruled out before surgical repair, and that in the presence of a mitral valve anomaly the anatomical correction should be given up in favor of a venous procedure.

Rafael Villavicencio, MD

A CONTROLLED STUDY OF THE ASSOCIATION BETWEEN ULCERATIVE COLITIS AND PSYCHIATRIC DIAGNOSES. Helger JE, Stillings, WA, Chammas S., et al. Digestive Diseases and Sciencies 1982; 27: 513-518.

Estos investigadores evaluaron la frecuencia y severidad de desórdenes mentales en 50 pacientes con colitis ulcerativa y en 50 pacientes controles con condiciones médicas crónicas no intestinales de edad, sexo y raza similar. Se hicieron exámenes siquiátricos considerados como confiables y válidos y los diagnósticos se basaron en criterios explícitos. El resultado principal del estudio fue que no hubo diferencia en la frecuencia de desórdenes mentales entre los dos grupos. Tampoco hubo relación entre la severidad de la colitis y de la severidad o frecuencia de problemas siquiátricos.

Angel Olazabal, MD

CITOMEGALOVIRUS ASOCIADO A MAL FUNCIONAMIENTO DEL SISTEMA INMUNOLOGICO: Gotllieb MS, et al. N Engl. J Med 1981, 305:1425; Masur H, et al. N. Engl J Med 1981, 305:1431; Siegal FP, et al. N Engl J Med 1981, 305:1439.

Ha ocurrido un aumento en la evidencia que asocia la infección por citomegalovirus (CMV) en adultos saludables con la presencia de inmunodeficiencia e infecciones oportunistas y neoplasias. Los estudios indican que los homosexuales constituyen una gran subpoblación en la cual la incidencia de infección por este virus es de hasta 94%. Estadísticas recientes muestran que las infecciones por el virus Epstein-Barr (EBV), mononucleosis, hepatitis B y por el virus herpes simplex (HSV) también son frecuentemente asociadas con este mismo grupo de personas.

Tres nuevos estudios nos proporcionan evidencia adicional a favor de la hipótesis de que existe una relación directa entre CMV y otras infecciones en hombres homosexuales. Gottlieb y colaboradores describieron los casos de cuatro pacientes homosexuales que desarrollaron pulmonía severa causada por *P. carinii,* además de infección con HSV y Candida. En cada caso se aisló CMV de varias secreciones y había evidencia de infección activa por CMV; en varios casos hubo evidencia de infección previa por CMV mononucleosis. Todos eran anérgicos y significativamente linfopénicos. Los linfocitos de estos pacientes no respondieron a antígenos comunes y sufrían intercambios marcados de supresores sobre linfocitos auxiliares (helper lymphocytes). Estos hallazgos inmunológicos son consistentes con CMV.

Masur y asociados evaluaron 11 pacientes con pulmonía producida por *P. carinii.* Todos eran drogadictos (7), homoxexuales (6), o ambos (2). La mitad de estos pacientes tenía historial del síndrome pseudo-mononucleosis (mononucleosis-like syndrome) previa a la pulmonía. Uno de ellos desarrolló sarcoma de Kaposi y otro desarrolló linfadenopatía angioinmunoblástica. Los estudios inmunológicos muestran una disminución en la cantidad y en la calidad de función de los linfocitos. Aunque no se realizaron estudios virales definitivos en todos los 11 casos, al menos uno de los pacientes murió por complicación pulmonar con CMV y *P. carinii.*

Siegel y colaboradores estudiaron cuatro homosexuales que desarrollaron infección con HSV con ulceraciones; en tres casos hubo evidencia de coexistencia con infección por CMV. Tres murieron y cuatro desarrollaron sarcoma de Kaposi. todos los pacientes eran anérgicos a antígenos comunes y además mostraban linfopenia con conteos que no excedían los 1,000. Como en reportes previos, las células T fueron suprimidas y hubo un mayor por ciento de células supresoras a células auxiliares (helper cells); hubo una disminución en la actividad de células asesinas (killer-cell) en contra de HSV.

Comentario: CMV es reconocida como una de las causas de malfuncionamiento del sistema inmunológico, tanto en animales como en el humano y tiene la capacidad de inducir linfopenia y suprimir muchas funciones expresadas por los linfocitos (lymphocyte-exppresed functions). CMV se trasmite sexualmente y es transportada en varios fluidos del cuerpo incluyendo el semen. La población de homosexuales parece estar altamente expuesta a este virus. Existe la interrogativa; ¿será CMV sólo el responsable por la inmunosupresión o existirá otro factor común en esta población que esté contribuyendo?

CMV suele estar acompañado de *P. carinii* en infecciones de neonatos y de individuos con inmunosupresión; y existe evidencia de que CMV puede crecer entre organismos de pneumocistis. Estudios *in vitro* con CMV han demostrado que éste es capaz de disminuir varias funciones inmunológicas permitiendo que otros virus y organismos invadan el cultivo. CMV puede ser transportado en el sistema reticuloendotelial por años, donde su influencia a largo plazo ha sido investigada recientemente en homosexuales con malfuncionamiento del sistema inmunológico.

C.H. Ramírez-Ronda, MD

A TRIAL OF TOPICAL ACYCLOVIR IN GENITAL HERPES SIMPLEX VIRUS INFECTIONS: Corey L., Nahmias A.J. et al., NEJM, 306, June 1982.

En este estudio realizado en la Universidad de Washington, los autores estudiaron la respuesta clínica de 77 pacientes con enfermedad genital por Herpes Simplex tratados con una nueva droga antiviral conocida como ACYCLOVIR. Los pacientes con primeros episodios de infección viral respondieron favorablemente al tratamiento con una disminución en la duración de la enfermedad y secreción de particulas virales comparado con placebo. En pacientes con herpes recurrente que eran varones, la droga logró una aceleración de la cura de las lesiones. En mujeres no hubo efecto en cuanto a mejora en este grupo con recurrencias.

Iván León, MD, F.C.C.P.

MSN MEDICAL SPECIALTIES NEWS

AMERICAN ACADEMY OF PEDIATRICS

AAP ANNUAL MEETING PROGRAM

The American Academy of Pediatrics (AAP) will hold its 1982 Annual Meeting October 23-28 in New York City, with headquarters at the Hilton Hotel.

The presentations will be given during plenary sessions which will be held Monday through Thursday of the meeting. Other plenary session highlights are recent developments in immunizing children against disease, the effects of divorce upon children, adolescent sexual and psychological issues, and herpes and hepatitis B infections in newborn infants.

The program will open on Saturday and Sunday with 16 postgraduate seminars. During these full-day sessions leaders in the field of child health care will discuss such topics as new developments in caring for high risk infants, medical marriages, the pediatrician as a family counselor, and the impact psychological and physical changes in adolescence have on prescribing of medications.

A series of round tables will be held Monday through Thursday. Highlights of these half-day sessions include how to help mothers breast feed, treating the gifted child, arthritis in young people, the father's role in infancy, and hypnosis in pediatric practice.

Other highlights of the meeting include programs to be held by the Academy's sections, groups of AAP members with specialized interests in such areas as child development, community health, sports medicine and neurology. Special workshops are scheduled for both new and veteran pediatricians. An array of scientific and technical exhibits, as well as product exhibits, also will be displayed.

Further information about registering for the meeting may be obtained by writing: Allison Waitley, Registration Supervisor, AAP, P.O. Box 1034, Evanston, Il. 60204.

aa BB AMERICAN ASSOCIATION OF BLOOD BANKS

NEW HEPATITIS B VACCINE FOR SALE

The newly-developed vaccine for Hepatitis B, approved by the Food and Drug Administration last year, is currently for sale by Merck, Sharp and Dohme, West Point, PA. The cost for the three-dose regimen is in the $100 range.

The vaccine is produced with virus fragments taken from the blood of carriers of the disease, unlike other vaccines that are grown from cells in the laboratory. It is the first vaccine licensed in the US that is manufactured directly from human blood and can be as high as 96 percent effective in preventing infection, tests have shown.

It is primarily targeted to "high risk" individuals, a group which includes health care workers, e.g. those who handle equipment in blood banks or kidney dialysis units, surgeons and dentists.

INTRAVENOUS IMMUNE SERUM GLOBULING NOW AVAILABLE

Immune serum globulin is useful for the treatment of patients with immune deficiencies secondary to hypogammaglobulinemia. These conditions include Bruton's sex-linked agammaglobulinemia, severe combined immunodeficiency or the acquired comon variable hypogammaglobulinemia associated with diseases such as chronic lymphocytic leukemia. A goal of therapy is often to maintain the lefvel of IgG above 250 mg%, since maintenance of immune globulin levels at or above this level has been shown to be associated with the decreased incidence of infection.

Immune serum globulin is prepared via alcohol fractionation of pooled plasma. This process removes most nonimmunoglobulin protein and provides a product with about 95% IgG[1]. In addition, the procesing procedure inactivates the hepatitis virus. This component is intended for intramuscular use since the IgG molecules form aggregates during preparation. These aggregated immunoglobulin molecules can activate complement via the alternative pathway and produce anaphylactic shock reactions.

Current practice is to administer intramuscular gamma globulin monthly to individuals with hypogammablobulinemia. These monthly injections, however, are painful and the injection of a large volume of liquid requires a fairly substantial muscle mass. Accordingly, patient compliance can be poor. Additionally a patient must have adequate hemostatic function to ensure that hemorrhage will not occur from the injection site. Systemic side effects from injection of intramuscular gamma globulin include anxiety, nausea and vomiting, cardiorespiratory instability, increased pulse, decreased blood pressure, malaise, flushing, facial swelling, cyanosis and loss of consciousness.[2] Some of these side-effects relate to allergic reactions while others are felt to be secondary to aggregated immunogloblin activating complement. The usual dose of immune serum globulin ranges from 0.2-0.6 ml/kg. In addition to pooled immune serum globulin there are also hyperimmune globulin preparations used to treat diseases such as polio, tetanus, measles, mumps, rabies, whoopinig cough, hepatitis B and herpes zoster. Rho(D) immune globulin is also useful for prevention of hemolytic disease of the newborn.

Since some patients cannot tolerate intramuscular injections of immune serum globulin on a monthly basis, researchers have been attempting to prepare gamma globulin suitable for intravenous administratin[3] [5]. The advantages would be that intravenous administration is relatively painless and one could infuse large volumes without concern for the size of the patient's muscle mass.

A product recently licensed for commercial use in the

United States, although similar products have been avaible in Europe for some time, is immune serum globulin (5%) suitable for intravenous administration. This product is prepared using a cold alcohol fractionation technique followed by reduction of the IgG molecules with dithiothreitol (to break the disulfide bonds) and then acetylated using iodoacetamide to prevent recombination of the disulfide bonds. The product is prepared in a 10% maltose solution and stabilized with 0.1 M glycine.

This material contains 96% IgG with a pH of 6.8 and a concentration of 50 mg of IgG per ml. The package insert states that the half life of the intravenous product is 22 days which is similar to the half life reported for the intramuscular preparation. By virtue of its intravenous route of administration this gamma globulin preparation does not require a two to seven day waiting period prior to the development of peak antibody titers as maximum titers are available immediately.

The manufacturer claims that this intravenous products retains the opsonic and complement fixing properties of the original IgG molecule but is free of anti-complementary activity. These properties are critical if the molecule is to function appropriately in vivo. The recommended dose is 0.1-0.2 grams/kg per month. Its use is contraindicated in patients with known IgG deficiencies and antibodies to IgA since there is some IgA present in this product and severe anaphylatic reactions could occur. Reported side effects, seen in about 10% of patients, are similar to those mentioned above for intramuscular gamma globulin preparations. Some of the side effects relate to the use of 10% maltose as well as the 0.1 glycine. At a meeting recently held on this topic at the National Institutes of Health, Pirofsky reported that the side effects associated with use of intravenous gamma globulin stabilized with 0.1 M glycine were much less than those side effects encountered when 0.3 M glycine was used to stabilize the preparation.

At the present time hypertimmune serum globulin preparations would not need to be administered on a chronic basis and there would not seem to be a need for intravenous administration of these products. One exception, however, would be the Rho immune globulin. At the present time one ml of this product given by intramuscular administration is sufficient to protect women who have been exposed to less than 30 ml of fetal blood during pregnancy. For the rare occasion, however, where a unit of Rho(D) positive blood is given to an Rho(D) negative individual, the use of large volumes of Rho immune globulin may be indicated. For such purposes intravenous preparations of Rho immune globulin could be of clinical value. Whether intravenous administration of large volumes of Rho immune globulin would consistently provide the same protective effect as intramuscular administration of small volumes, however, remains to be determined.

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american society of internal medicine

BEHAVIOR MODIFICATION: SHOULD PHYSICIANS SAY "YES"?

Techniques of behavior modification —ranging from biofeedback mechamisms to hypnosis to psychotherapy— are here to stay, but if and when physicians should acept them are questions yet to be answered, according to William Campbell Felch, MD, editor of "The Internist", the magazine of the American Society of Internal Medicine (ASIM).

"Doctors tend to be comfortable with innovations introduced by peers and can speedily adopt even revolutionary strategies providing those strategies are endorsed by colleagues within the establishment," Felch writes in his opening remarks in the June 1982 issue of **The Internist,** "But the school of behavior modification has yet to achieve that imprimatur. Much of its theory and some of its techniques have not been sufficiently subjected to the kind of rigorous, randomized control studies that are demanded by academia before approval is given."

Many of the spokesmen for the school of behavior modification "come across as enthusiastic advocates instead of dispassionate scientists, crusaders striving to win acceptance through anecdotal testimony masquerading as science." Although he admits that many of the advocates have suitable educational degrees and hold respectable positions at medical schools, he likens others —those without degrees, professional license and scientific credentials— to "carnival hawkers."

Two authors agree with Felch, suggesting that many of the new-fangled approaches to modifying patients' behavior aren't what they're cracked up to be. ASIM Past President James A. Collins, Jr., MD, says that although some forms of behavior modification may work to a degree, "good personal public relations" and "a platform of faith" are more effective in the long run. "The physician who takes the necessary extra time to go into great detail about a problem with his patient can acomplish as much as or more than many of the techniques currently in vogue."

Donald J. Merwin, vice president for programs and acting chief executive officer of the National Center for Health Education, maintains that the only approach to changing people's behavior that seems capable of producing lasting results is education. In his article, Merwin explains that a well-planned patient education program should be based on an assessment of the patient's needs, have specific measurable objectives and use a variety of methods to get its messages across.

AMERICAN COLLEGE OF EMERGENCY PHYSICIANS

ACEP TAKES STAND ON NUCLEAR WEAPONS DEVELOPMENT

The American College of Emergency Physicians has announced plans to work to halt nuclear weapons proliferation.

According to the College's President B. Ken Gray, M.D., "The ACEP Board of Directors agreed to petition political leaders to find an effective means of halting further development, testing and deployment of nuclear weapons. We would like to see worldwide nuclear disarmament."

Because emergency physicians would be responsible for treating victims of thermo-nuclear incidents, the Board also agreed to provide educational offerings to its members, with information about the medical consequences and appropriate medical management of victims of a thermo-nuclear incident," Dr. Gray said. "However, we feel our members should be prepared to treat casualties where necessary."

The College currently has almost 11,000 physician members in the United States, Canada and Puerto Rico. Among its goals is the improvement of patient care in the emergency department. The College offers continuing medical education programs to emergency physicians in order to reach this goal.

AMA NEWS

HEALTH RISK SEEN IN CHILDREN SEDATED FOR CAT SCANS

Youngsters sedated to keep them still during a CAT scan have developed serious, and in some instances life-threatening, drug-induced reactions.

In a collaborative study of Boston-area pediatric patients, researchers at Harvard Medical School and Boston University School of Medicine found that 13 of 106 children who were sedated prior to a CAT (Computed Axial Tomography) scan of the head developed adverse reactions. The risk appeared greatest when multiple drugs and high doses were used in combination, although the youngest infants reacted severely to normal doses of a single drug.

Allen A. Mitchell, MD, director of the Pediatric Drug Surveillance Program rum by the two Boston schools, was principal investigator for the study, which appears in the May 7 issue of JAMA.

The CAT scan itself involves only a low dose of radiation but, as the Boston study shows, drugs used to keep the young patients motionless during the 15 to 30 minute procedure caused a wide range of problems from vomiting to life-threatening respiratory arrest. Children with more severe reactions required treatment with another drug to reverse the effects of the narcotics. There were no fatalities, however, and no apparent long-term consequences.

The children who developed adverse reactions to the premedication ranged in age from two days to 15 years and received up to five drugs in combination. Life-threatening events occurred in only the four infants younger than three months. Two of these infants received only single injections of morphine.

"We're not suggesting that CAT scans be avoided," Mitchell said in a separate interview. "The CAT scan is a noninvasive procedure that we've found invaluable in assessing problems like congenital malformations, brain tumors and injuries to the head. It is more accurate and less traumatic than older diagnostic techniques it replaces.

"What's important is choosing the right drugs and dosages for sedating the youngsters before a scan and then carefully watching them for signs of reaction both during the scan and afterward on the hospital ward."

FETAL EFFECTS OF MATERNAL ALCOHOL USE

The AMA Council on Scientific Affairs calls for research on fetal risk of abnormality associated with moderate and minimal maternal alcohol consumption. Research is also called for to determine whether there is a level of consumption below which fetal risk is virtually noexistent. Until such determination is made, according to the Council, physicians should continue to counsel women that their safest course is to abstain from drinking alcoholic beverages during pregnancy.

Alcohol is a drug that crosses the placenta and affects the fetus. Investigators agree that fetal abnormalities are associated with excessive maternal drinking, but there is controversy over the dangers of moderate and minimal alcohol use.

The current medical literature regarding fetal effects of maternal alcohol use includes seven epidemiological studies involving 65,000 pregnant women. Most ethnic, racial and socioeconomic groups are represented, as are drinking practices ranging from abstinence to alcohol abuse.

Several hundred cases of fetal alcohol syndrome have been reported in association with maternal alcohol abuse. Infants with fetal alcohol syndrome usually have facial structure abnormalities, deficient prenatal and postnatal growth, and central nervous system dysfunction, including mild to moderate mental retardation. Fetal alcohol syndrome occurs in about 1 in 750 live births in the general population — comparable to the incidence of spina bifida and Down's syndrome— but in 30 to 40 percent of infants of alcoholics mothers.

Fetal alcohol syndrome occurs throughout the world, but its incidence has been disproportionately high among American Indians, lower socioeconomic groups and children of older mothers. This higher incidence may result from greater alcoholism and alcohol abuse among women in these groups.

Other fetal risks associated with heavy maternal drinking include higher frequencies of stillbirths and spontaneous abortions.

Studies of moderate maternal alcohol use have been inconclusive because of inconsistent definition of "moderate" consumption levels and because of possible underestimation of consumption based on self-reports of drinking. There is also a lack of data on patterns of drinking —for example, constant consumption as opposed to intermittent or "spree" drinking.

There is conflicting evidence regarding the association of moderate drinking with malformations, premature delivery and decreased birth weight. More convincing evidence, although still inconclusive, links moderate drinking with spontaneous abortions, and with behavior dysfunction, poor mental and motor development, and impaired conditioning in the newborn.

Some investigators suggest that fetal risk is proportional to maternal alcohol intake, with minor developmental abnormalities occurring at lower levels of consumption and major abnormalities at higher levels.

The Council outlines the following issues requiring further investigation:

- The biochemical mechanisms by which alcohol produces fetal defects.
- Duration of alcohol-related birth defects and dysfunctions.
- Delayed effects of maternal alcohol use appearing in older children.
- Influence of poor nutrition, drug use, smoking, poverty and other variables on findings from studies of maternal drinking.
- Influence of duration and pattern of drinking on fetal outcome.
- Effects of different kinds of alcoholic beverages.
- Effects of paternal alcohol use prior to conception.

The full report of the AMA Council on scientific Affairs on the fetal effects of maternal alcohol use, from which this backgrounder is adapted, was approved during the AMA Annual Meeting, June, 1982, by majority vote of the House of Delegates. By this action, that report has become official policy of the American Medical Association.

SHORTER HOSPITAL STAY FOUND SAFE FOR PATIENTS WITH UNCOMPLICATED HEART ATTACK

Two weeks of hospitalization is just as safe as three weeks for patients who have had an uncomplicated heart attack, according to a report in the May, 1982 issue of **Archives of Internal Medicine.**

In the first long-term follow-up of heart attack patients assigned to either a two-week or three-week treatment program, Harvard Medical School researchers could find no differences between the two groups with respect to survival, heart disease-related deaths, frequency or severity of anginal chest pains, use of medication, subsequent heart attacks, and other selected heart disorders. Adolph M. Hutter, Jr., MD, Associate Professor of Medicine at Harvard school, was principal investigators for the study, which reassessed 123 patients (including 53 who had died) an average of eight years after their initial hospitalization.

One interesting difference, unrelated to the length of hospital stay, did show up in the findings: Patients who were smokers at the time of their heart attack and who stopped smoking afterward had a significantly higher survival rate than patients who continued to smoke.

The Harvard study corroborates the safety of recommendations made in 1976 by the National Heart, Lung, and Blood Institute for hospitalization of patients with uncomplicated heart attack: four days of bed rest followed by five to ten days of progressive activity.

NEW STUDY FINDS NO LINK BETWEEN VAGINAL SPERMICIDES AND MAJOR BIRTH DEFECTS

Contrary to findings in a previous study reported last year, new research indicates that children born to women who become pregnant while using vaginal spermicide contraceptives have no increased risk of birth defects.

Writing in the May 7, issue of **JAMA**, Samuel Shapiro, MD, reports no significant difference in the overall frequency of major malformations in children exposed to spermicide creams, foams and jellies before birth compared to children who were not exposed. Shapiro is Research Professor of Epidemiology at Boston University of Medicine.

Shapiro analyzed data obtained in the late 1950s through the mid-1960s on more than 50,000 pregnant women. In this group, he found more than a thousand women who had used spermicides before and for some time after becoming pregnant.

Separate analyses of statistics on women who had used spermicides containing mercury and on those who had used spermicides without mercury showed that major malformations occurred in 20, or 2.8 percent, of 889 children born to the first group of women and in 10, or 2.2 percent, of 462 children born to the second group. (Spermicides containing mercury are no longer marketed.)

These rates were no higher than that for children whose mothers had not used spermicides. Shapiro concludes that the nonmercurial spermicides currently in use do not increase the overall risk of major birth defects.

His results, however, contradict the findings of Hershel Jick, MD, from a Seattle study reported in the April 3, 1981, issue of **JAMA** .

According to an accompanying editorial in the current **JAMA** by Godfrey P. Oakley, Jr., MD, of the Centers for Disease Control in Atlanta, Jick had found a twofold increase in the incidence of major malformations among children born to spermicide users. He had also found specific increases in Down's syndrome, hypospadias (a malformation of the penis), tumors and limb deformities. Shapiro reports no excess of these abnormalities among children born to spermicide users surveyed for the Boston University study.

"Our overall findings are encouraging," Shapiro said in a separate interview. "But many birth defects occur so infrequently that they were not seen in our study in large enough numbers to provide reliable statistics. We could not exclude the possibility that spermicide use might increase the risk of specific malformations.

IT'S A LONG, HARD RUN TO BETTER HEART HEALTH

Running to promote cardiovascular health does work — but you may have to run at least 10 miles a week for almost a year before the benefits become apparent.

Researchers at Stanford University School of Medicine studied the effects of a one-year running schedule on lipids (fats) in the blood, on physical fitness and on body fat content. Paul T. Williams, MS, of Stanford's Heart Disease Prevention Program, was principal author of a report appearing in the May 12 **JAMA** that assesses findings in 48 healthy, previously sedentary men aged 30 to 55 years compared to 33 control subjects who did not participate in the exercise program.

Higher blood levels of high-density lipoprotein cholesterol (HDL-C) and lower blood levels of low-density lipoprotein cholesterol (LDL-C), both measurements associated with a reduced risk of heart attack, were not seen until after nine months of running at least 10 miles per week.

More encouraging news for reluctant runners is that changes in physical fitness and body fat content occurred earlier and at lower levels of activity than alterations in HDL-LDL distribution.

Fitness, measured by treadmill endurance and oxygen uptake tests, improved as early as three months into the running program at activity levels of five miles per week or less. Treadmill endurance leveled off after six months, regardless of increased running mileage, but oxygen uptake capacity continued to improve.

Decreases in body fat content also became apparent afer only three months of exercise and continued, particularly at high activity levels, to the end of the one-year program.

Williams notes that because the study evaluated only healthy middle-aged men, the results might not apply to people with other characteristics.

EYE DISEASE IN DIABETICS IS FREQUENTLY MISDIAGNOSED

Diabetic retinopathy, the leading cause of adult blindness in the United States, can be arrested if recognized and treated early enough. But in more than 60 percent of cases, diagnosis of the disease may be missed by the physicians who care for most diabetic patients, according to statistics from a Pennsylvania study reported in JAMA, June 18, 1982.

Diabetic retinopathy was diagnosed correctly in just 39 percent of examinations performed by 23 primary care physicians and specialists in the study. Internists, residents and diabetologists had correct diagnosis rates of 27 percent, 31 percent and 36 percent, respectively. General ophthalmologists and retinal specialists had correct diagnosis rates of 52 percent and 70 percent, respectively. Elliott J. Sussman, MD, assitant professor of medicine at the Hospital of the University of Pennsylvania, headed the investigation which involved 11 patients.

The cause of diabetic retinopathy is unclear, but physicians believe that the degenerative process begins early in the course of the diabetes and develops for years before becoming clinically apparent. The earliest signs include tiny aneurysms on the retinal blood vessels and minute hemorrhages that result when the aneurysms rupture. A more advanced stage termed proliferative retinopathy is marked by the formation of new retinal blood vessels, often in an uncontrolled, spaghetti-like tangle, which can hemorrhage into the vitreous humor. The final consequence can be partial or total blindness.

Sussman and colleagues report that internists missed 52 percent of the diagnoses of proliferative retinopathy, residents missed 50 percent, diabetologists missed 33 percent, and general ophthalmologists missed 9 percent, while retinal specialists did not miss any. It is at this stage of the disease that treatment by laser photocoagulation of the proliferating blood vessels can reduce the risk of progressive loss of vision, according to Jay S. Skyler, MD, associate professor of medicine and pediatrics at the University of Miami School of Medicine, in an accompanying editorial.

In the Diabetic Retinopathy Study, a federally sponsored controlled clinical trial carried out between 1971 and 1979, laser photocoagulation reduced the incidence of severe visual impairment from 36.7 percent in untreated eyes to 16.6 percent in treated eyes over a five year period, Skyler notes.

Sussam found, as an unexpected result of his study. That ophthalmologists tended to overdiagnose proliferative retinopathy. His data suggest that proliferative disease actually will not be present in 70 percent of the patients who are given that diagnosis. Sussman and Skyler agree that patients with suspected proliferative retinopathy should be referred to retinal specialists for confirmation of the diagnosis by retinal photographs and x-rays.

Because diabetic retinopathy develops slowly in juvenile-onset insulin-dependent diabetics, ophthalmologic examinations rarely reveal the disease in the early years. Still, Skyler advises, these patients should be examined yearly for retinopathy, initially by the primary physician. After about eight to ten years, or earlier if there is suspicion of retinopathy, the examinations should be performed by an ophthalmologist. In older patients who develop diabetes, the examinations should begin about four to eight years after onset of the disease. Diabetics should seek routine eye care from an ophthalmologist rather than an optometrist, Skyler says.

EDUCACION MEDICA CONTINUADA

THE FIFTH ANNUAL CURRENT CONCERNS IN ADOLESCENT MEDICINE

Program Chairman: I. Ronald Shenker, MD
Chief of Adolescent Medicine
The Department of Pediatrics
Long Island Jewish-Hillside Medical Center

This fifth annual course will deal with important topics in adolescent medicine today. The three major headings: Adolescent Health Care Delivery, Orthopedic and Sports Medicine and Health Risk of the Adolescent encompass such topics as the Legal Rights of Adolescents and Parental Involvement in Adolescent Health Care (parents' rights versus patient confidentiality) - The Clinical Assessment of Knee Pain and Scoliosis - Teenage Abortion (a clinical discussion of the epidemiology of abortion since 1962) - The Psychiatric Aspects of Teenage Suicide (the third leading death in America today) and Immunodeficiency Syndrome (a new disease of male homosexuals).

As an organization accredited for continuing medical education, Long Island Jewish-Hillside Medial Center certifies that this activity meets the criteria for 14 credit hours in Category 1 from the Accreditation Council for Continuing Medical Education (ACCME).

For further information: Ann J. Boehme, Continuing Education Coordinator, Long Island Jewish-Hillside Medical Center, New Hyde Park, New York 11042. Telephone: (212) 470-2114.

SAN DIEGO RADIOLOGY RESEARCH AND EDUCATION FOUNDATION

A continuing medical education course: **Musculoskeletal Disease: New Diagnostic Concepts and Modalities** will be presented February 14-17, 1983 at the Hotel Del Coronado in San Diego, California. The program will include discussion of degenerative, traumatic, metabolic neoplastic, infectious and articular disorders of the musculo skeletal system. The newest techniques including computed tomography and arthrography will be stressed.

The Program Directors are Donald L. Resnick, M.D. and Jose Guerra, Jr., M.D. The faculty inclues Harry Genant, M.D. of the University of California School of Medicine at San Francisco, California and Thomas Goergen, M.D., Jose Guerra, Jr., M.D., Saskia Hilton, M.D., Donald Resnick, M.D., and Kathyrn F. Witztum, M.D. of the University of California School of Medicine at San Diego, California.

The Course is accredited for 19 hours Category I AMA certification program. The fee for the course is $300.00 or $200.00 for physicians in training.

For further information, please contact Mary J. Ryals, Suite 101, 10855 Sorrento Valley Road, San Diego, CA 92121. Tel (714) 452-4722.

CLINICAL CYTOPATHOLOGY FOR PATHOLOGISTS - POSTGRADUATE COURSE

The Twenty-fourth **Postgraduate Institute for Pathologists in Clinical Cytopathology** is to be given at The Johns Hopkins University School of Medicine and The Johns Hopkins Hospital, Baltimore, Maryland, April 18-29, 1983. The full two week program is designed for pathologists who are Certified (or qualified) by the American Board of Pathology(PA), or their international equivalents.

It will provide an intensive refresher in all aspects of the field of Clinical Cytopathology, with time devoted to newer techniques, special problems, and recent applications. Topics will be covered in lectures, explored in small informal conferences, and discussed over the microscope with the Faculty. Self-instructional material will be available to augment at individual pace. A loan set of slides with texts will be sent to each participant for home-study during March and April before the Institute. Credit hours 125 in AMA Category 1.

Application is to be made before February 2, 1983. For details, write: John K. Frost, M.D., 610 Pathology Building, The Johns Hopkins Hospital, Baltimore, Maryland 21205, U.S.A.

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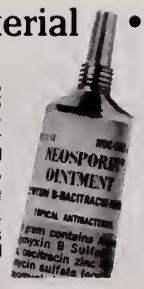

DESCRIPTION: Each gram contains: Aerosporin® (Polymyxin B Sulfate) 5,000 units, bacitracin zinc 400 units, neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs; in tubes of 1 oz and ½ oz and 1/32 oz (approx.) foil packets.

INDICATIONS: *Therapeutically* (as an adjunct to systemic therapy when indicated), for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically,* the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

CONTRAINDICATIONS: Not for use in the eyes or in the external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of its components.

WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

ADVERSE REACTIONS: Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.

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Before prescribing, please consult complete product information, a summary of which follows:

Indications and Usage: For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli, Klebsiella-Enterobacter, Proteus mirabilis, Proteus vulgaris, Proteus morganii.* It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. *Note:* The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

For acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over other antimicrobials. Limited clinical information presently available on effectiveness of treatment of otitis media with Bactrim when infection is due to ampicillin-resistant *Haemophilus influenzae*. To date, there are limited data on the safety of repeated use of Bactrim in children under two years of age. Bactrim is not indicated for prophylactic or prolonged administration in otitis media at any age.

For acute exacerbations of chronic bronchitis in adults due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in physician's judgment it offers an advantage over a single antimicrobial agent.

For enteritis due to susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

Also for the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

Contraindications: Hypersensitivity to trimethoprim or sulfonamides; patients with documented megaloblastic anemia due to folate deficiency; pregnancy at term; nursing mothers because sulfonamides are excreted in human milk and may cause kernicterus; infants less than 2 months of age.

Warnings: BACTRIM SHOULD NOT BE USED TO TREAT STREPTOCOCCAL PHARYNGITIS. Clinical studies show that patients with group A β-hemolytic streptococcal tonsillopharyngitis have higher incidence of bacteriologic failure when treated with Bactrim than do those treated with penicillin. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

Precautions: *General:* Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function. Bactrim may prolong prothrombin time in those receiving warfarin; reassess coagulation time when administering Bactrim to these patients.

Pregnancy: Teratogenic Effects: Pregnancy Category C. Because trimethoprim and sulfamethoxazole may interfere with folic acid metabolism, use during pregnancy only if potential benefits justify the potential risk to the fetus.

Adverse Reactions: All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. *Blood dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic reactions:* Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *CNS reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous reactions:* Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

Dosage: Not recommended for infants less than two months of age.

URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN, AND ACUTE OTITIS MEDIA IN CHILDREN:

Adults: Usual adult dosage for urinary tract infections—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days. Use identical daily dosage for 5 days for shigellosis.

Children: Recommended dosage for children with urinary tract infections or acute otitis media—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. Use identical daily dosage for 5 days for shigellosis.

For patients with renal impairment: Use recommended dosage regimen when creatinine clearance is above 30 ml/min. If creatinine clearance is between 15 and 30 ml/min, use one-half the usual regimen. Bactrim is not recommended if creatinine clearance is below 15 ml/min.

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Usual adult dosage: 1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 14 days.

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Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

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1. Rubin RH, Swartz MN: *N Engl J Med 303* 426-432, Aug 21, 1980. **2.** Data on file, Medical Department, Hoffmann-La Roche Inc.

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Please see previous page for summary of product information.